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ANALYSIS OF SITES AND CAUSES OF TREATMENT FAILURES IN SQUAMOUS CELL CARCINOMAS OF THE ORAL CAVITY*

By GILBERT H. FLETCHER, M.D.,† WILLIAM S. MACCOMB, M.D.,‡
and ERNEST J. BRAUN, M.D.§
HOUSTON, TEXAS

THE tumors originating on the anterior two thirds of the tongue, floor of the mouth, buccal mucosa, upper and lower gums and hard palate form separate clinical entities with a natural history, histologic behavior and inherent characteristics of their own. Valuable data might be lost to analysis if they were grouped together for the sake of greater statistical significance.

This study is limited to 224 patients with squamous cell carcinoma of the oral cavity, previously untreated, referred to the M. D. Anderson Hospital for the purpose of treatment. Patients not treated, because the disease was too advanced or the patients refused treatment, are counted as failures. Hard palate squamous cell carcinomas, too few for analysis, are omitted. The analysis of upper gum lesions is less detailed due to the small number of cases.

The anatomic definition of the various sites is based on conventional concepts. The subdivision of the tongue into two parts, the anterior two thirds or mobile portion (the portion in front of the circumvallate papillae) and the posterior third, or base of the tongue, is universally accepted. The base of the tongue originates embryologically from oropharynx segments, and the tumors arising from it have a biologic behavior similar to those of the oropharynx. The posterolateral border of the tongue, that is, the portion which is in front of the circumvallate papillae at the level of the anterior faucial pillar, is included in the anterior two thirds of the tongue because the mucous membrane is the same as the oral cavity mucous membrane. If the whole tongue is involved, the case is assigned to either the anterior two thirds or the base of the tongue, depending upon the main area of involvement and ulceration,

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† The University of Texas M. D. Anderson Hospital and Tumor Institute, Section of Radiotherapy, Houston, Texas.
‡ The University of Texas M. D. Anderson Hospital and Tumor Institute, Department of Surgery, Head and Neck Service, Houston, Texas.
§ The University of Texas M. D. Anderson Hospital and Tumor Institute, Section of Radiotherapy, Houston, Texas. Presently at White Memorial Hospital, Department of Radiotherapy, Los Angeles, California.

the anaplasticity of the tumor, and the size, multiplicity, and location of neck lymph nodes. These criteria of allocation are based on the biologic behavior of the tumors at each site.

STAGING

Staging of the extent of disease at various sites was so arranged as to make a comparison of results between treatment centers possible, as well as to help determine the prognosis. These staging systems are based on findings when the patient is first seen and may not be particularly suited for an analysis of sites and causes of treatment failures. For instance, this practice applied to oral cavity squamous cell carcinomas implies that a patient first seen, without neck lymph node involvement, is staged in the "no lymph node metastases" category. Some of those patients develop lymph node involvement at a later date and a percentage will die from uncontrolled neck disease, the cause of failure being the metastatic aggressiveness.

The staging of neck lymph node metastases must be made at the end of the period of follow-up used in the analysis. The staging of the primary lesion is made on original findings and never changed. In order to correlate the biologic and natural history of the disease at the primary site, in the neck, and at a distance, the extensions of the primary lesion and of the metastatic disease in the neck must be staged separately.

In many systems of staging, Stage I cases are those in which the primary lesion is limited to the organ of origin. This method cannot apply to the oral cavity because, for instance, a 1 cm. lesion on the lateral border of the tongue and another lesion occupying the whole tongue are both confined to the organ of origin, but are, respectively, an early and a very advanced lesion. Furthermore, the same dimensions cannot be used as criteria of staging for the primary lesions at all the anatomic sites. A 5 cm. diameter lesion on the lateral border of the tongue has a good chance for local control, whereas a lesion of the same size on the anterior floor of the mouth is nearly incurable. The varying types of surrounding structures involved must also be given different weights in staging.

Size and extensions to supporting structures are both considered in the staging of the primary lesions, with variations to fit the anatomic sites (Table I). The classification used in this report is based on the recommendations of the International Committee for Stage-Grouping in Cancer as prepared at the Seventh International Congress in Copenhagen in July, 1953. Table II shows the distribution of the cases treated according to anatomic sites.

A code (Table I) representing the significant events in the evolution of the cases can be graphically portrayed on dual staging charts of the primary lesions and metastatic neck lymph nodes. The operational charts contain much pertinent information, and have been made for each anatomic site. All patients treated, either by surgery or by irradiation, are included.

Table III is the chart for tumors of the anterior two thirds of tongue analyzed at five years. Similar charts have been made for the other sites, but for three years' follow-up only because the number of cases exposed to five year follow-up was not large enough. Valid information is obtained at three years, as the incidence of local recurrences and/or neck disease for the squamous cell carcinomas of the oral cavity is small after three years.

ANALYSIS OF DATA

A considerable amount of data can be derived from the dual staging charts. In Table IV the incidence of lymph node metastases with respective survival rates is shown for the anatomic sites, with the exception of the upper gum lesions which are not numerous enough for analysis. Lesions of the anterior two thirds of the tongue, floor of the mouth, gum and buccal mucosa have a decreasing tendency to metastasize. Consequently, the salvage rate for metastatic neck disease is lowest in

TABLE I

STAGING OF PRIMARY CARCINOMA

	T_1	T_2	T_3	T_4
Anterior ⅔ of Tongue	Less than 3 cm. in diameter	3 cm.–5 cm. with possible minimal extension to floor of mouth or deep muscle infiltration	5 cm. to half tongue with possible limited extension to floor of mouth	More than ½ tongue or massive extension to floor of mouth with involvement of mandible
Buccal Mucosa	Less than 3 cm. in diameter	3 cm.–5 cm. with minimal extension to adjacent structures: muscle, gingiva, faucial pillars	Greater than 5 cm. with limited extension to adjacent structures	Massive invasion
Gums	Less than 3 cm. in diameter	(1) 3 cm.–5 cm. minimal extension to floor of mouth or buccal mucosa (2) No bone involvement	Greater than 5 cm. or pressure bone defect	Massive invasion or (moth-eaten) bone infiltration
Floor of Mouth	Less than 2 cm. in diameter	2 cm.–4 cm. with minimal extension, up to 2 cm. thick	Greater than 4 cm. or fixed to periosteum. More than 2 cm. thick but still limited invasion of root of tongue	Massive invasion of root of tongue or bone

STAGING OF LYMPH NODE METASTASES

N_0 No lymph node enlargement
N_1 Single small to moderate size (less than 3 cm.)
N_2 Large, movable lymph node or multiple unilateral lymph nodes (more than 2 cm.)
N_3 Fixed large unilateral lymph node or bilateral lymph nodes (more than 2 cm.)
M Distant metastases when first seen
(The lymph node metastases classification is based on lymph node involvement appearing at any time. For instance, if a patient has first a unilateral lymph node involvement, then later a lymph node involvement on the opposite side, it is then N_3)

Code:

NT	No treatment
RT	Refused treatment
PAL	Palliative treatment
●	No evidence of disease
OP	Operative death or death during postoperative period
P	Primary lesion uncontrolled
P (S or R)	Recurrence of primary lesion successfully treated by surgery or radiation
N	Neck lymph node metastases uncontrolled
DM	Distant metastases
P or DM or N, alone	Failure at that site alone. Addition of letters means combination of sites of failures
SP	Second primary lesion
ID	Intercurrent disease
A	Age 80 or more
Surg.	Surgery
0	Alive less than 1 year
1	Alive 1–2 years
2	Alive 2–3 years
3	Alive 3–4 years
4	Alive 4–5 years
5	Alive 5 or more years
C	Commando operation
MR	Marginal resection
O	Treated with orthovoltage radiation
S	Treated with supervoltage radiation

Primary Lesion Control: No palpable or visible evidence of disease at primary site if patient alive; or if dead, shortly prior to death. Unhealed necrosis is counted as failure.
Neck Lymph Node Metastases Control: The same criteria as for primary lesions.

patients having involvement of the anterior two thirds of the tongue and highest for patients with lesions of the buccal mucosa. There are no patients alive even at three years with bilateral neck lymph node metastases from tongue lesions, but there is a significant salvage rate for those with lymph nodes metastases associated with floor of mouth lesions. There are not enough cases of buccal mucosa and lower

TABLE II

DISTRIBUTION BY SIZE OF PRIMARY LESIONS AND NECK LYMPH NODE METASTASES OF 206 CASES TREATED OF SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY

	Anterior ⅔ of Tongue 62 Treated				Floor of Mouth 46 Treated				Buccal Mucosa 35 Treated				Upper Gum 11 Treated				Lower Gum 52 Treated			
	N_0	N_1	N_2	N_3	N_0	N_1	N_2	N_3	N_0	N_1	N_2	N_3	N_0	N_1	N_2	N_3	N_0	N_1	N_2	N_3
T_1	11	2	0	0	10	0	0	3	7	0	1	0	0	0	1	0	7	3	1	0
T_2	8	4	1	2	5	1	1	1	6	0	1	0	1	0	0	0	7	3	0	0
T_3	9	2	5	5	9	4	2	3	6	2	2	2	0	3	0	0	12	4	1	2
T_4	2	3	2	6	3	0	1	3	5	0	2	1	1	0	2	3*	5	3	3	1

* One with distant metastases when first seen.

SUMMATION

	N_0	N_1	N_2	N_3	Total
T_1	35	5	3	3	46
T_2	27	8	3	3	41
T_3	36	15	10	12	73
T_4	16	6	10	14	46
	114	34	26	32	206

TABLE III

ANTERIOR TWO THIRDS OF TONGUE
62 TREATED

(55 RADIATION—7 SURGERY)

	N_0	N_1	N_2	N_3
T_1 (13)	*Alive*: 7; 2 Surg. — *Dead*: 1 (ID); 1 Surg. (ID)	*Alive*: 1 Surg. — *Dead*: 1 (P+N)	42: Alive 25; Dead 17 (8 ID)	*Alive* — *Dead*
T_2 (15)	*Alive*: 3; 2 Surg. — *Dead*: 2 (ID); 1 (no data)	*Alive*: 2 (1 S) — *Dead*: 1 (N); 1 (ID)	*Alive*: 1 (S) — *Dead*	*Alive* — *Dead*: 2 (ID) (N+DM)
T_3 (21)	*Alive*: 6 (1 S) — *Dead*: 3 (3 ID)	*Alive*: 1 — *Dead*: 1 Surg. (DM)	*Alive* — *Dead*: 5: 2 P+N; 2 N; 1 Surg. P+N	*Alive* — *Dead*: 5: 1 P+N; 2 N; 1 P+N+DM; 1 DM
T_4 (13)	*Alive*: 1 (S) — *Dead*: 1 (P)	*Alive*: 3 — *Dead*	*Alive* — *Dead*: 2 (P+N); 20: Alive 4; Dead 16 (2 ID)	*Alive* — *Dead*: 6: 1 DT*; 3 P+N; 1 N; 1 P+N+DM
	21→30←9	7→11←4	1→8←7	0→13←13

* Delirium tremens.

TABLE IV

ORAL CAVITY SQUAMOUS CELL CARCINOMA TREATED BY SURGERY OR RADIATION OR BOTH COMBINED

206 CASES

Treated	Anterior ⅔ of Tongue 62—5 Years	Floor of Mouth 46—3 Years*	Buccal Mucosa 35—3 Years*	Lower Gum 52—3 Years*
No lymph node metastases at any time	30 67% Alive	27 63% Alive	24 80% Alive	31 70% Alive
Lymph node metastases	32 25% Alive	19 58% Alive	11 46% Alive	21 43% Alive
Total	47% Alive	61% Alive	71% Alive	60% Alive

* Five year results are 5–10% below three year results as calculated by Mary C. Macdonald, Biometrician in the Section of Radiotherapy.

NOTE: Because of the small numbers, the statistical significance of the figures is limited, more so for the "no lymph node metastases" and "lymph node metastases" groups.

gum tumors with bilateral neck lymph node metastases to draw any conclusions.

Thirty-nine patients with massive (T_4) lesions were treated for possible cure and 7 for palliation only. Of the 39 radically treated, 13 have lived three years or more, 11 without any evidence of disease. The best results have been obtained in the cases presenting anterior two thirds of the tongue and buccal mucosa lesions, because radical irradiation could be used due to the excellent tolerance of those two structures. No T_4 case of the floor of the mouth has reached three years without disease; one patient is living with disease at three years. Lesions of the floor of the mouth, due to their anatomic location, are, size for size, harder to control. This explains the small difference in salvage rate between the group with lymph node metastases and the group without lymph node metastases.

The sites of treatment failures are given in Table v. The differential diagnosis of a recurrence at the primary site or in the neck or both is difficult in some cases when the recurrence is close to the primary lesion in the scar of a composite operation. Those cases have usually been counted as recurrence at the primary site and in the neck, although some are probably recurrences

TABLE V

SITES OF FAILURE IN 224 CASES OF ORAL CAVITY SQUAMOUS CELL CARCINOMA REGISTERED

	Anterior ⅔ of Tongue	Floor of Mouth	Buccal Mucosa	Lower Gum	Upper Gum	Totals
No. of patients registered	68	51	38	55	12	224
No. of patients dead	(5 years)	(3 years)	(3 years)	(3 years)	(3 years)	
	39	24	15	28	8	114
No treatment (too advanced or refused)	6	5	3	3	1	18
Treated palliatively			3	3	1	7
No data as to cause of death	1		1	1		3
Intercurrent disease (ID)	10	6	4	3	2	25
Distant metastases only (DM)	2	3		1		6
Neck uncontrolled and distant metastases (N+DM)	1			1	1	3
Neck uncontrolled alone (N)	6	2		2		10
Primary lesion uncontrolled and distant metastases (P+DM)				2		2
Primary lesion and neck uncontrolled and distant metastases (P+N+DM)	2					2
Primary lesion and neck uncontrolled (P+N)	10	4	1	8	3	26
Primary lesion uncontrolled alone (P)	1	6	3+2 PAL	4+3 PAL		19

TABLE VI

FAILURES OF CONTROL OF PRIMARY LESIONS IN T_1, T_2, AND T_3 CASES

	T_1				T_2				T_3			
	Tongue	Floor of Mouth	Buccal Mucosa	Lower Gum	Tongue	Floor of Mouth	Buccal Mucosa	Lower Gum	Tongue	Floor of Mouth	Buccal Mucosa	Lower Gum
Surgery												
No. of Patients	4	4	1	7	1	0	2	5	2	7	3	14
Failure of Control	0	0	0	2	0	0	1	0	1	4	1	7
Radiation												
No. of Patients	9	9	7	4	13	8	5	5	19	11	9	5
Failure of Control	1	0	0	0	0 (2(S))*	0 (2(S))*	0	0	4 (1(S))*	1 (2(S))*	0	3
Significant Complications	0	1	0	0	0	1	0	1	0	4	0	0

* Recurrences following radiation therapy successfully excised.

SUMMATION

Radiation and Surgery

	T_1	T_2	T_3
No. of Patients	45	39	70
Failures	3	1	21

only at the primary site. A recurrence after either a surgical procedure or irradiation, treated successfully by the other discipline, is not counted as a treatment failure because the primary lesion is ultimately controlled. The treatment of several of those patients was actually planned on the basis of the sequential use of radiation and surgery.

Table v shows that approximately 40 per cent of the causes of death are not dependent on the treatment of the primary and neck disease. The majority of the deaths due to an uncontrolled primary lesion alone are in the T_4 cases, without neck lymph node metastases. Uncontrolled disease in the neck alone, or in conjunction with lack of control of the primary lesion, is a common cause of treatment failure. In several instances further treatment could have been given to patients for the primary lesion but it was not indicated because of massive disease in the neck. If the neck lymph node metastases are no larger than 3 cm. in diameter, a very satisfactory salvage rate is obtained. Nineteen of 33 such cases are alive at three years or more without evidence of disease. Multiple unilateral lymph node metastases or lymph nodes larger than 3 cm. in diameter, darken the prognosis. Only 6 out of 29 patients are alive at three years or more.

A detailed analysis (Table VI) of the control of the primary lesions, excluding the T_4 cases, shows that failure to control the primary lesion by surgery or radiation or both combined is rare, with the exception of cases of lower gum lesions.

METHODS OF TREATMENT

The management of the squamous cell carcinomas of the oral cavity must be flexible enough to meet the varied situations created by the anatomic sites and their extensions. Even if one discipline, either surgery or radiation, is ordinarily the

treatment of choice for a particular site there are exceptions. Many cases must be judged upon their individual merits.

Early superficial lesions, especially on the basis of leukoplakia or if close to bone, are often excised. The tumors of the anterior two thirds of the tongue, of the buccal mucosa and of the floor of the mouth have been treated essentially by interstitial radium implants. The tumors of the lower gum have more often been handled surgically than by radiation therapy, and almost all tumors of the upper gum have been surgically treated. There has long been an established program of combining radiation and surgery in the treatment of advanced lesions. Radical irradiation can sterilize the more radiosensitive peripheral extensions and therefore render the surgical excision of a residuum of tumor more successful and less crippling. The healing of the mucous membranes, even after radical irradiation, is satisfactory. A number of recurrences following irradiation has been successfully excised by local surgical procedures (Table VI). Irradiation of surgical recurrences is not as systematically successful.

Neck disease has been managed primarily by radical neck dissection. On some occasions, when the lymph nodes were large or close to the primary lesion, radiation was given for growth restraint until the time of the neck dissection.

DISCUSSION

From the analysis of 224 cases of oral cavity squamous cell carcinomas, previously untreated, the following points stand out:

1. A closely integrated program of radiation and surgery, with the use of interstitial radium implants for most lesions of the tongue, buccal mucosa and floor of the mouth, is an efficient way of controlling the primary lesions. Flexibility as to the choice of either discipline is maintained and, in the more advanced lesions, the sequential use of the two improves results. Even in the massive, or T_4, category, approximately one third of the patients have survived three years or more.

2. A more systematic use of radiation and surgery is being investigated for the lower gum lesions.

3. Metastatic aggressiveness is the main cause of treatment failure when lymph nodes, even unilateral, are multiple or more than 3 cm. in diameter. Various modalities of irradiation with skin-sparing beams (cobalt 60 and cesium 137 units) prior to radical neck dissection are under trial.

SUMMARY

The mere number of patients alive does not explain the causes of death and therefore does not indicate the areas of weakness in the methods of treatment.

Separate staging codes for the primary lesions and neck lymph node metastases are utilized to produce operational charts which reveal detailed information as to the sites and clinical circumstances in which there has been failure to control the primary lesion, the neck disease, or both. From this analysis, programs for better management of those cases which fall in the unsatisfactory categories can be investigated.

Gilbert H. Fletcher, M.D.
The University of Texas M. D. Anderson Hospital and Tumor Institute
Texas Medical Center
Houston 25, Texas

END RESULTS AND CAUSES OF FAILURE IN TREATMENT OF INTRAORAL CARCINOMA*

By LEWIS W. GUISS, M.D.,† *and* IAN MACDONALD, M.D.‡
LOS ANGELES, CALIFORNIA

THE authors' total experience in the management of intraoral carcinoma arising in several anatomic sites is presented in such a way as to permit comparison with other similar efforts. Further, the success or failure of treatment is analyzed with reference to the size of the primary lesion and the occurrence of lymph node metastases. Finally, it is hoped that a critical review of the causes for defeat in the treatment programs in the past may indicate areas for improving future end results.

MATERIAL

All cases accepted for treatment in the authors' private practice for either curative or palliative management during the study period are included, even though recommended therapy was refused by the patient. Many of the cases represent patients previously, partially or unsuccessfully, treated with persistent or recurrent disease. The study group includes all cases seen for five or more years.

METHOD

The varied clinical data were reduced as accurately as possible to common denominators with reference to size and location of lesions, status of lymph node involvement, method of treatment, control of disease, causes of death and reasons for therapeutic failure. This information was transferred to punch cards for analysis.

DEFINITION OF TERMS

Reference to the treatment of the primary lesion when irradiation is indicated as the modality of treatment implies that it was the sole controlling factor. Many irradiation failures were subsequently definitively and successfully treated by surgery though the converse is seldom true. When surgery is designated as the treatment of choice, it does not exclude the possiblity of previous irradiation. Lymph node metastases are histologically proved metastases. The status of the lymph node involvement is based on the entire study period and includes metastases, unilateral or bilateral, at any time in the course of the disease. The curative management of clinical lymph node involvement has been by radical neck dissection, frequently in continuity with the primary lesion. Irradiation has been primarily applied to lymph node metastases only in palliative management.

Success or failure is determined by the patient's status on the fifth anniversary of this treatment. For example, if the patient is free of disease at the end of five years he is counted as a "five year control" even though he might subsequently die of intercurrent disease. Patients succumbing to other causes, free of carcinoma, in less than five years, are listed as dying of intercurrent disease. All operative deaths are included as deaths from intraoral carcinoma.

CARCINOMA OF THE TONGUE

All cases of epidermoid carcinoma arising in or involving the anterior two-thirds of the tongue are included. As will be noted in Table 1, a total of 65 patients were registered, 56 of whom completed definitive treatment to their primary lesions, 25 by irradiation and 31 by surgery, the latter group comprising irradiation followed by surgery.

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† Associate Clin. Prof. Surgery, University of Southern California School of Medicine.
‡ Clin. Prof. Surgery, University of Southern California School of Medicine.

Table I

FIVE YEAR RESULTS FOR CARCINOMA OF THE TONGUE

			Surgery	Irradiation	Total		
65 Total	9 no treatment	7 too advanced					Alive 27
		2 refused					
	56 treated	controlled	16	11	27	49 (determinate)	
		dead of carcinoma	10	12	22		
		dead of intercurrent disease	5	2	7	7 (indeterminate)	
							Dead 38

"Cure Rates"

Absolute	27/65 = 41.6%
Relative	27/56 = 48.2%
Determinate	27/29 = 55.1%

The "five year cure rates" obtained vary from the *absolute* rate (41.6 per cent) based on all patients seen, through the *relative* figure (48.2 per cent) based on patients treated, to the usually reported figure based on *determinate* cases of 55.1 per cent and which excludes those dying of intercurrent disease from the calculation. This variation emphasizes the need for careful definition of the cure rate being used in reporting. In Table II the end results are itemized by the size of the primary lesion and stage of lymph node involvement. It is immediately apparent that the small primary carcinoma without lymph node involvement is readily dealt with by either surgery or irradiation but 1 of 33 so treated dying of carcinoma (distant metastases). When the problem of unilateral lymph node involvement is added to that of the primary lesion, the cure rate drops abruptly to 11.7 per cent. Three failures were due to distant metastases, the remaining 12 equally divided between persistent local disease and unconfined lymph node involvement.

In the cases of bilateral lymph node involvement, the one cure is difficult to explain; the remaining 5 died of extension of the primary carcinoma or its disseminated spread, as might be expected.

CARCINOMA OF THE ALVEOLAR RIDGE

All cases of epidermoid carcinoma arising in the mucosa over the alveolar ridge and which have been treated five or more years ago are included. Many had prior treatment elsewhere either by irradiation, cauterization or limited surgical procedures and were referred here with persistent or recurrent disease. Definitive treatment to the primary lesion was almost invariably by surgery, frequently in continuity with lymph node dissection. Though several of these cases had primary irradiation of their lesions, this remained uniformly unsuccessful and surgical resection became necessary either for persistent disease or radiation necrosis.

The five year salvage (Table III) for this group is not as satisfactory as that for carcinoma of the tongue, and this deficiency invites scrutiny. From Table IV it is noted that, while the distribution of the cases with regard to lymph node involvement is essentially identical with the carcinoma of the tongue group, the primary lesions were on the average considerably larger. The reason for failure in the potentially curable patients (excluding those with bilateral lymph node involvement) was almost invariably lack of control of the primary lesion, and not of the lymph node

TABLE II

FIVE YEAR RESULTS FOR CARCINOMA OF TONGUE BY SIZE OF PRIMARY LESION AND STATUS OF LYMPH NODE INVOLVEMENT

Size of Lesion	33 No Lymph Node Involvement (58.9%)			17 Unilateral Lymph Node Involvement (30.4%)			6 Bilateral Lymph Node Involvement (10.7%)		
	Alive	Dead		Alive	Dead		Alive	Dead	
		I.D.	Ca.		I.D.	Ca.		I.D.	Ca.
<1 cm.	2R 7S	2S	1S(DM)						
1 cm. to 2 cm.	2R 5S	1R 2S	1S(OP)	1S		1S(DM) 1R(N) 2R(DM)			1R(P) 1S(N)
2 cm. to 3 cm.	4R 4S					1S(N) 2R(N)	1R		2S(N)
>3 cm.				1S		1S(P) 4R(P) 1R(N)			1R(P)
Not stated		1R 1S				1S(P) 1S(N)			
Total	24	7	2	2		15	1		5
"Cure Rates"									
Relative	24/33=72.7%			2/17=11.7%			1/6=16.6%		
Determinate	24/26=92.2%			2/17=11.7%			1/6=16.6%		

Code to Tables: R=Primary treated by irradiation. S=Primary treated by surgery. I.D.=Death from intercurrent disease, free of carcinoma. Ca.=Death from intraoral carcinoma. P=Death from uncontrolled primary carcinoma. N=Death from uncontrolled lymph node metastases. DM=Death from distant metastases (blood borne). OP=Operative death.

metastases. This might be summarized as "too little, too late" with reference to the primary lesion.

CARCINOMA OF THE BUCCAL MUCOSA

This group comprises all epidermoid carcinomas arising in the buccal mucosa treated five or more years ago (Table v). Half of the primary lesions were treated surgically and half by irradiation with essentially equal success. The modality selected for treatment seemed not as important as the size of the primary lesion and its extension to adjacent structures. Treatment of metastatic lymph nodes was by radical neck dissection, though not a single case with positive lymph nodes was controlled (Table vi). However, when the causes for failure are analyzed, it becomes readily apparent that it was inability to control the primary carcinoma in every case but one, instead of extension to the lymph nodes that resulted in death. If any extension of surgical management were to improve the end results for buccal carcinoma, it would have to be directed to the primary lesion and not to the lymph nodes. On the other hand, one could infer that lymph node metastases develop late and only in association with incurable primary buccal lesions. This latter assumption is strengthened by the fact that all but one case without lymph node involvement were controlled satisfactorily.

TABLE III

FIVE YEAR RESULTS FOR CARCINOMA OF THE ALVEOLAR RIDGE

35 Total	6 no treatment; disease far advanced or distant metastases				Alive 11
	29 treated surgically	controlled	11	27 (determinate)	
		died of carcinoma	16		
		died of intercurrent disease	2	2 (indeterminate)	Dead 24

"Cure Rates"
Absolute 11/35=31.4%
Relative 11/29=37.9%
Determinate 11/27=40.7%

CARCINOMA OF THE FLOOR OF MOUTH

Only 22 patients with epidermoid carcinoma of the floor of the mouth were first seen over five years ago and permit evaluation. Included are cases with lesions that apparently arose in the floor of the mouth but had extended into the adjacent tongue and/or alveolar ridge (Table VII). The primary lesion was treated by surgery in 12 cases and by irradiation in 8. Control of the primary carcinoma was achieved by both modalities in all but one instance, suggesting that either method could be equally effective in this anatomic site, other factors probably determining success or failure. Radical neck dissection successfully controlled lymph node metastases in 2 of 7 patients developing them. Since treatment failures (Table VIII) consisted of 2 cases of persistent primary disease, 1

TABLE IV

FIVE YEAR RESULTS FOR CARCINOMA OF THE ALVEOLAR RIDGE BY SIZE OF PRIMARY LESION AND STATUS OF LYMPH NODE INVOLVEMENT

Size of Lesion	17 No Lymph Node Involvement (58.6%)			9 Unilateral Lymph Node Involvement (31.0%)			3 Bilateral Lymph Node Involvement (10.3%)		
	Alive	Dead		Alive	Dead		Alive	Dead	
		I.D.	Ca.		I.D.	Ca.		I.D.	Ca.
<1 cm.	1S								
1 cm. to 2 cm.	3S		1S(P)			1S(P) 1S(DM) 1S(OP)			
2 cm. to 3 cm.	3S	1S	1S(P)		1S	1S(OP)			2S(N)
>3 cm.	3S		3S(P)			4S(P)			1S(N)
Not stated	1S								
Total	11	1	5	0	1	8	0	0	3
"Cure Rates" Relative	11/17=64.7%			0/9=0.0%			0/3=0.0%		
Determinate	11/16=68.7%			0/8=0.0%			0/3=0.0%		

TABLE V

FIVE YEAR RESULTS FOR CARCINOMA OF THE BUCCAL MUCOSA

28 Total	2 no treatment; far advanced disease with distant metastases						Alive 15
	26 treated		Surgery	Irradiation	Total		
		controlled	8	7	15	23 (determinate)	
		dead of carcinoma	3	5	8		
		dead of intercurrent disease	2	1	3	3 (indeterminate)	
		total	13	13	26		
							Dead 13

"Cure Rates"
Absolute 15/28 = 53.6%
Relative 15/26 = 57.7%
Determinate 15/23 = 65.2%

TABLE VI

FIVE YEAR RESULTS FOR CARCINOMA OF THE BUCCAL MUCOSA BY SIZE OF PRIMARY LESION AND STATUS OF LYMPH NODE INVOLVEMENT

Size of Lesion	19 No Lymph Node Involvement (73.2%)			7 Unilateral Lymph Node Involvement (26.8%)		
	Alive	Dead		Alive	Dead	
		I.D.	Ca.		I.D.	Ca.
<1 cm.	3S 1R	2S				
1 cm. to 2 cm.	4S 1R					1S(OP) 1R(P)
2 cm. to 3 cm.	3R	1R	1R(P)			1S(P) 1R(P)
>3 cm.	1S 2R					1S(OP) 1R(OP) 1R(N)
Total	15	3	1	0	0	7
"Cure Rates" Relative 15/19 = 78.9% Determinate 15/16 = 93.7%				0/7 = 0.0% 0/7 = 0.0%		

TABLE VII

FIVE YEAR RESULTS FOR CARCINOMA OF THE FLOOR OF MOUTH

			Surgery	Irradiation	Total		
22 Total	2 no treatment	1 suicide					Alive 11
		1 far advanced					
	20 treated	controlled	6	5	11	17 (determinate)	
		dead of carcinoma	3	3	6		
		dead of intercurrent disease	3		3	3 (indeterminate)	
							Dead 11

"Cure Rates"
Absolute 11/22=50.0%
Relative 11/20=55.0%
Determinate 11/17=64.7%

operative death, and 3 cases of uncontrolled lymph node metastases, it is not possible to make valid suggestions for improving end results based on small numbers.

CARCINOMA OF THE HARD PALATE

Only 8 cases of epidermoid carcinoma arising in the mucosa of the hard palate were encountered in the review period, of

TABLE VIII

FIVE YEAR RESULTS FOR CARCINOMA OF THE FLOOR OF MOUTH BY SIZE OF PRIMARY LESION AND STATUS OF LYMPH NODE INVOLVEMENT

Size of Lesion	13 No Lymph Node Involvement (65.0%)			7 Unilateral Lymph Node Involvement (35.0%)		
	Alive	Dead		Alive	Dead	
		I.D.	Ca.		I.D.	Ca.
<1 cm.	1S	2S				1R(P)
1 cm. to 2 cm.	2S 3R	1S		1S		1R(OP)
2 cm. to 3 cm.			1S(P)			2S(N) 1R(N)
>3 cm.	1R			1R		
Total	9	3	1	2	0	5
"Cure Rates" Relative 9/13=69.2% Determinate 9/10=90.0%				2/7=28.6% 2/7=28.6%		

TABLE IX

FIVE YEAR RESULTS FOR CARCINOMA OF THE HARD PALATE

			Surgery	Irradiation	Total		
8 Total	2 no treatment	1 far advanced					Alive 4
		1 refused					
	6 treated	controlled	2	2	4	—5 (determinate)	
		dead of carcinoma	1 (DM)		1		
		dead of intercurrent disease	1		1	—1 (indeterminate)	Dead 4

"Cure Rates"
Absolute 4/8 = 50.0%
Relative 4/6 = 66.6%
Determinate 4/5 = 80.0%

which 6 were treated. Such a small group has no statistical significance and the cases are included only to complete the study (Table IX). The primary disease was uniformly controlled surgically in 4 and by irradiation in 2. None developed lymph node metastases. Two cases, one with intercurrent disease (leukemia) and one with distant blood borne metastases, did not survive.

DISCUSSION

In Table X the five year cure rates for all *treated* cases are summarized according to the organ sites surveyed. The over-all success rates, both relative and based on

TABLE X

CARCINOMA OF THE ORAL CAVITY
SUMMARY OF THE FIVE YEAR SURVIVAL RATES FOR TREATED CASES

	Anterior Two-thirds of the Tongue	Alveolar Ridge	Buccal Mucosa	Floor of Mouth	Hard Palate
No lymph node involvement Alive	33 (58.9%) 24 (72.7%)	17 (58.6%) 11 (64.7%)	19 (73.2%) 15 (78.9%)	13 (65.0%) 9 (69.2%)	6 (100%) 4 (66.6%)
Lymph nodes involved unilaterally Alive	17 2 (11.7%)	9 0 (0.0%)	7 0 (0.0%)	7 2 (28.6%)	
Lymph nodes involved bilaterally Alive	6 1 (16.6%)	3 0 (0.0%)			
Total with lymph node involvement	23 (41.1%)	12 (41.3%)	7 (26.8%)	7 (35.0%)	
Cures with lymph node involvement	3 (13.1%)	0 (0.0%)	0 (0.0%)	2 (28.6%)	
Over-all "cure rates" Relative Determinate	 48.2% 55.1%	 37.9% 40.7%	 57.7% 65.2%	 55.0% 64.7%	 66.6% 80.0%

Table XI

FACTORS RESPONSIBLE FOR FAILURE OF TREATMENT IN CARCINOMA OF THE ORAL CAVITY

Sites	Cases without Lymph Node Involvement					Cases with Lymph Node Involvement				
	I.D.	OP	P	N	DM	I.D.	OP	P	N	DM
Tongue	7	1			1			8	9	3
Alveolar ridge	1		5			1	2	5	3	1
Buccal mucosa	3		1				3	3	1	
Floor of mouth	3		1				1	1	3	
Hard palate	1				1					
Total	15	1	7		2	1	6	17	16	4

determinate cases, were higher than the authors had anticipated. When a more critical inspection is made however, it is noted that these higher than average cure rates reflect a relative preponderance of cases (64 per cent) which never developed lymph node metastases and in which thus a higher salvage rate should be expected. Any sense of satisfaction in regard to the over-all figures is lost on viewing the results achieved in patients with lymph node metastases (only 10 per cent five year salvage). This deficiency indicates a possible productive area for further investigation.

The cause for each failure in the treatment program is indicated in Table XI. Among the patients without lymph node involvement the greatest loss occurred in those who developed intercurrent disease, obviously beyond the reach of medical control. The only possible area of treatment improvement would appear to be in those dying of uncontrolled or recurrent primary carcinoma, but on further investigation it was found that these lesions were either so large or already recurrent when first seen that little hope could be entertained for improving the record.

In the group with lymph node metastases, the patients dying of their primary lesions (17) were also those with processes frequently of large size and already recurrent when first seen. The only category where any significant improvement would seem reasonably possible appears to be among those succumbing to uncontrolled lymph node metastases, free of primary carcinoma and distant metastases.

During the period of this review, it was an accepted policy that radical neck dissections were to be done only in cases with clinical evidence of lymph node metastases. In retrospect, it becomes obvious that because of this rule, many patients were lost due to uncontrollable lymph node metastases which developed later. Frequently, by the time carcinomatous spread is clinically evident in the neck, the process has already passed beyond the capabilities of a radical neck dissection and the patient dies of contralateral or distant metastases or more often of recurrence in the dissected side of the neck. The authors for some time have been aware of the fact that, too often, clinical evidence of metastases in the cervical lymph nodes signifies eventual incurability of the carcinoma. Because of this, they have slowly been forced to the conclusion that if the distressing record of death from lymph node metastases is to be notably improved, neck dissection should be done before irrefutable evidence of the presence of metastases develops. Moreover, when a lateralized primary lesion has been controlled by either surgery or irradiation, serious consideration should be given to elective neck dissection on the homolateral side. If the size, grade and history of the primary

TABLE XII

ELECTIVE VERSUS THERAPEUTIC NECK DISSECTIONS

	Elective				Therapeutic						
	No.	NED*	D(I.D.)	D(P)	No.	NED*	D(I.D.)	D(P)	D(N)	DDM	DOP
Tongue	6	6			16	2		3	8	3	
Alveolar ridge	7	4	1	2	12		1	5	5	2	
Buccal mucosa					4			3			1
Floor of mouth	2	1		1	7	2		1	3		1
Total	15	11	1	3	39	4	1	12	16	5	2

* NED=No evidence of ca.

lesion make the likelihood of eventual metastatic disease seem remote, elective dissection is omitted. If, however, these same considerations point to the probability of eventual lymph node involvement, elective dissection is advised and, if the patient is willing, completed. Such a neck dissection is not "prophylactic" in any sense of the word; the procedure does not prevent metastases to the cervical lymph nodes. The operation is "elective" in that it is done earlier in the clinical course of the disease prior to palpable and visible evidence of involvement rather than waiting until surgical intervention is mandatory.

The mere fact that the pathologist may return a negative report on such specimens does not mean that metastases have not occurred. Mounting evidence suggests that in most malignant lesions the process of metastatic dissemination is a continuous one and occult malignant cells are present in every such neck, undetectable by present relatively crude sampling methods. The record for "elective" versus therapeutic dissections for this group of cases is shown in Table XII. Of 15 patients who had neck dissections done despite clinical absence of metastases and negative pathologic reports, many as part of continuity procedures, 12 remained free of any evidence of subsequent lymph node involvement and 3 died of recurrent primary carcinoma. Among the 39 cases which underwent therapeutic operations, there were but 4 five year survivors, and one dying of intercurrent disease. Almost half of the deaths in this group were caused by progression of uncontrolled lymph node metastases. Any significant improvement in the end results of this study group would have to be achieved among those succumbing to carcinomatous extension to their lymph nodes, probably by applying the principle of "elective" radical neck dissection.

SUMMARY

Epidermoid carcinoma of the intraoral cavity is a relatively curable disease if treated before there are metastases. Determinate five year cure rates around 90 per cent may be expected for cases without lymph node involvement.

Treatment of intraoral carcinoma complicated by spread to the lymph nodes is much more difficult, the five year salvage figures for this group being but 10 per cent.

Depending on the ratio of cases with and without lymph node involvement, the over-all five-year salvage should average about 50 per cent for the various intraoral sites anterior to the tonsillar pillars.

Earlier application of "elective" radical neck dissection to cases regarded as likely to develop lymph node metastases sometime in their clinical course appears to offer potential improvement in eventual cure rates.

Lewis W. Guiss, M.D.
University of Southern California
School of Medicine
Los Angeles, California

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EVALUATION OF FAILURES IN TREATMENT OF ORAL CANCER*

By ARTHUR G. JAMES, M.D.
COLUMBUS, OHIO

THIS study deals with all cases of cancer of the anterior tongue, floor of mouth, buccal mucosa, gingiva and the palate, on the files of the Tumor Registry* of the Cancer Clinic, Ohio State University Health Center, between 1945 and 1956. All cases were considered whether or not they were treated. The study is concerned primarily with the causes of failures in this group.

MATERIAL

One hundred and thirty-six cases were available for study, five or more years after treatment and 218 cases that were three or more years after treatment. The cases were classified as to the extent of the primary carcinoma, and presence and extent of involvement of metastases. Staging was carried out according to the following plan.

TREATMENT

In general, the lesions were treated by surgery when feasible. Those that were not surgically approachable were treated by irradiation. Radiation therapy was also used as an adjunct to surgery when the lesion could not be completely resected.

Surgical Management. Small primary lesions of the tongue, floor of mouth, gingiva, buccal mucosa and palate were treated by simple wide excision when lymph node involvement was not present. When positive lymph nodes were present in the neck, in-continuity procedures were executed. When the lesions were large, neck dissection and resection of the primary lesion were usually performed, whether or not neck lymph node involvement was present. A mandibulectomy was performed when the primary lesion occurred in the gingiva and when the primary lesion in the other sites extended to such close proximity to the mandible to make that resection advisable. The justification for this more radical type of surgery even though positive lymph nodes were not present in such situations have been described elsewhere[3] and will not be dwelled upon in this paper.

For the uncomplicated metastatic lesion of the neck, with the primary carcinoma controlled, the treatment of choice was radical neck disection. Indications for radical neck dissection have been noted in the medical literature from time to time. It is interesting to note that these indications have changed over the course of time. For example, Duffy[1] in 1940 listed the following indications: (1) primary lesion is controlled; (2) the primary lesion is limited to one side of the oral cavity; (3) the primary lesion is shown to be of highly differentiated cell type; (4) cervical metastases are present and limited to one group of lymph nodes or lymph nodes in two contiguous triangles; (5) capsule of lymph nodes is not perforated by carcinoma; (6) opposite side of neck is free of metastases; (7) no distant metastases are present; (8) patient is in good general condition.

The first indication should be modified to read, "Primary lesion is controlled or plans should be made to remove the primary lesion at the time the neck dissection is performed." This combined surgical procedure—*i.e.*, removal of the cervical lymph nodes plus resection of the primary lesion, has been developed during the past fifteen years and has become feasible primarily

* Follow-up information by Edward E. Wieben, Statistician, Tumor Registry, Columbus Cancer Clinic, Ohio State University Health Center.

* Presented at the Forty-first Annual Meeting of the American Radium Society, Hot Springs, Virginia, April 6–8, 1959. Part of the Colloquium: Causes of Failure in the Treatment of Cancer of the Oral Cavity, moderated by Dr. William S. MacComb.
From the Department of Surgery, Ohio State University Health Center, Columbus, Ohio.

STAGING OF PRIMARY CARCINOMA

	P_1	P_2	P_3	P_4
Anterior two-thirds of tongue	Less than 3 cm.; no more than 1 cm. thick	3 cm.–5 cm. with possible minimal extension to floor of mouth or deep muscle infiltration	5 cm. to one-half of tongue with possible limited extension to floor of mouth	More than one-half of tongue or massive extension to floor of mouth with involvement of mandible
Floor of mouth	Less than 2 cm.; no more than 1 cm. thick	2 cm.–4 cm. with minimal extension, up to 2 cm. thick	Greater than 4 cm. or fixed to periosteum. More than 2 cm. thick but still limited invasion of root of tongue	Massive invasion of tongue or bone
Gingiva	Less than 3 cm.; superficial	(1) 3 cm.–5 cm. minimal extension to floor of mouth or buccal mucosa (2) No bone involvement	Greater than 5 cm.; or pressure bone defect	Massive or (moth-eaten) bone infiltration
Buccal mucosa	Less than 3 cm.; no more than 1 cm. thick	3 cm.–5 cm. with minimal extension to adjacent structures; muscle, gingiva, faucial pillars	Greater than 5 cm. with limited extension to adjacent structures	Massive
Palate	Less than 3 cm.	3 cm.–5 cm. minimal extension to adjacent structures	Greater than 5 cm. with limited extension to adjacent structures	Massive

STAGING OF LYMPH NODE METASTASES

N_0 No palpable lymph node
N_1 Single small to moderate size (less than 3 cm.) lymph node
N_2 Large, movable lymph node or multiple unilateral lymph nodes (more than 2 cm.)
N_3 Fixed, large unilateral lymph node or bilateral lymph nodes (more than 2 cm.)
N_D Distant metastases when first seen
(The lymph node classification was based on lymph nodes appearing at any time. For instance, if a patient had first a unilateral lymph node then later a lymph node on the opposite side, it would be classified as N_3)

because of the more frequent use of blood transfusions and the development of antibiotics. Prior to these developments, patients subjected to such procedures often died of shock or sepsis.

The second, third and sixth indications can be discussed in one paragraph. Actually, these statements were made because, at that time, it was not recognized that bilateral neck dissections could be performed. Also, it was thought that if a person developed lymph node involvement in the opposite side of the neck, the prognosis was hopeless. These misconceptions have been disproved with time, and it is now known that it is possible to salvage some patients who develop lymph node involvement in the contralateral neck, or have bilateral involvement at the time of surgery.

Indication number 5 is not now generally accepted. It is impossible to tell by palpation whether or not a localized area of metastasis is surgically resectable, and if surgical resection is carried out, whether the patient will remain free of disease. Accordingly, when there is any doubt, the patient should be given the benefit of that doubt, and resection attempted.

Indication number 7 is still accepted.

The only time this indication is not considered is when a neck dissection is advocated on a palliative basis.

Indication number 8 does not imply as much limitation as in the past. Actually, the patient should be checked to be sure that his general condition is satisfactory. However, it has become more the impression that age alone is not a contraindication to such surgery and the developments of blood transfusions, antibiotics and better anesthesia have made it possible to operate upon patients who could not have tolerated surgery twenty years ago.

If the primary tumor is resectable, then the neck dissection should be accompanied by surgical resection of the primary tumor. The finding of a nonresectable mass, whether primary or metastatic, is indication for some form of irradiation.

Radiation Therapy. Radiation therapy for metastatic cancer in the neck was used primarily as an adjunct to surgery. This was either in the form of high voltage external therapy or interstitial radioactive isotopes.

The use of radioactive isotopes will be discussed further because of their relative newness. One of the chief advantages of using these agents is the feasibility of loading them in a thin flexible nylon applicator. We have used Co^{60}, Au^{198}, and Ir^{192}. The preparation and method of using these agents have been described elsewhere.[2] Briefly, the method of usage is as follows: Guide needles are first implanted into the tumor tissue in question. Care must be taken to prepare a proper implant pattern by regular placement of the needles. The needles are then threaded with the ends of the nylon applicators and, as the needles are pulled through, the applicators follow the same pattern. Long applicators are used with the distal end loaded with the radioactive sources. The isotopes are kept in lead containers until the time of pulling the radioactive sources into place. Within a few minutes the radioactive material can be positioned. The radiation pattern is superior to the usual "free-hand" method and the exposure hazard to the operating personnel is negligible.

TABLE I

ORAL CANCER TREATMENT

	136 Cases with Five Year Follow-up		218 Cases with Three Year Follow-up	
	45 Survivals	91 Failures	91 Survivals	127 Failures
Surgery	35	55	74	78
Radiation Therapy	7	23	10	27
Surgery plus Radiation Therapy	3	9	7	11
No Treatment	0	4	0	11

Table I indicates the therapeutic procedures employed in the individual cases.

STATISTICAL ANALYSIS

Tables II through XXI list the relative information for each particular site.

CARCINOMA OF ANTERIOR TONGUE

Table II illustrates that 27 cases of carcinoma of the anterior tongue qualified for five year study with 15 failures and 52 cases qualified for three year study with 26 failures. Tables III–V give the type of treatment, survivals and the causes of failure.

CARCINOMA OF FLOOR OF MOUTH

Table VI indicates that 17 cases of carcinoma of the floor of mouth qualified for five year study with 13 failures and 26 cases qualified for three year evaluation with 16 failures. The pertinent data as to modality of treatment, survivals and causes of failure are listed in Table VII–IX.

CARCINOMA OF GINGIVA

Table X shows that in the group of carcinoma of the gingiva 44 cases were five or more years after the initial treatment with 28 failures and 69 cases were at least three years after treatment with 39 failures. The particulars are given in Tables XI–XIII.

(*Text continued on page 427*)

TABLE II

CARCINOMA OF ANTERIOR TONGUE

Over-all		No Lymph Nodes Involved		Lymph Nodes Involved	
27—5 year cases 12—survivals	52—3 year cases 26—survivals	10—5 year cases 9—survivals	24—3 year cases 20—survivals	17—5 year cases 3—survivals	28—3 year cases 6—survivals

	N_0		N_1		N_2		N_3		N_D	
	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases
17—5 year cases 11—living P_1 30—3 year cases 20—living	10 cases 1 dead 1 P.F.	20 cases 3 dead 2 P.F. 1 N.F.	1 case 1 dead 1 N.F.	3 cases 2 dead 2 N.F.	2 cases 1 dead 1 P+N	3 cases 2 dead 1 N.F. 1 P+N	4 cases 3 dead 2 N.F. 1 P+N	4 cases 3 dead 2 N.F. 1 P+N	0	0
8—5 year cases 1—living P_2 16—3 year cases 5—living	0	3 cases 0 dead	0	0	3 cases 2 dead 1 N.F. 1 P.A.	5 cases 4 dead 2 N.F. 1 P.A. 1 P+N	4 cases 4 dead 2 N.F. 1 P.A. 1 P+N	7 cases 6 dead 4 N.F. 1 P.A. 1 P+N	1 case 1 dead 1 N.F.	1 case 1 dead 1 N.F.
1—5 year case 0—living P_3 2—3 year cases 1—living	0	0	0	0	0	0	1 case 1 dead 1 N.F.	2 cases 1 dead 1 N.F.	0	0
1—5 year case 0—living P_4 4—3 year cases 0—living	0	1 case 1 dead 1 N.T.	0	0	0	1 case 1 dead 1 P+N	1 case 1 dead 1 N.T.	2 cases 2 dead 2 N.T.	0	0

Code: P.F.—Primary Failure; N.F.—Node Failure; N.T.—Not Treated; P+N—Primary plus Node Failure; P.A.—Palliative Attempt.

TABLE III

CARCINOMA OF ANTERIOR TONGUE

TREATMENT

	27 Cases with Five Year Follow-up		52 Cases with Three Year Follow-up	
	12 Sur-vivals	15 Fail-ures	26 Sur-vivals	26 Fail-ures
Surgery	9	9	23	14
Radiation Therapy	2	3	2	6
Surgery plus Radiation Therapy	1	1	1	2
No Treatment	0	2	0	4

TABLE IV

CARCINOMA OF ANTERIOR TONGUE

SURVIVALS

	27 Cases with Five Year Follow-up		52 Cases with Three Year Follow-up	
No Lymph Nodes Involved	10		24	
Survivals	9	90%	20	83.3%
Primary Lesion				
<3 cm.		90%		85%
>3 cm.		No cases		75%
Lymph Nodes Involved	17		28	
Survivals	3	17.6%	6	21.4%
All Cases	27		52	
Survivals	12	44.4%	26	50%

TABLE V

CARCINOMA OF ANTERIOR TONGUE
CAUSES OF FAILURE

	27 Cases with Five Year Follow-up 15 Failures	52 Cases with Three Year Follow-up 26 Failures
Primary Failure	1	2
Lymph Node Failure —Neck	7	13
Lymph Node Failure —Distant	1	1
Primary plus Lymph Node Failure	3	5
Not Treated	1	3
Palliative Attempt	2	2
Intercurrent Disease	0	0

TABLE VII

CARCINOMA OF FLOOR OF MOUTH
TREATMENT

	17 Cases with Five Year Follow-up		26 Cases with Three Year Follow-up	
	4 Sur-vivals	13 Fail-ures	10 Sur-vivals	16 Fail-ures
Surgery	3	7	7	8
Radiation Therapy	1	4	2	6
Surgery plus Radiation Therapy	0	2	1	2
No Treatment	0	0	0	0

TABLE VI

CARCINOMA OF FLOOR OF MOUTH

Over-all		No Lymph Nodes Involved		Lymph Nodes Involved	
17—5 year cases 4—survivals	26—3 year cases 10—survivals	5—5 year cases 2—survivals	8—3 year cases 5—survivals	12—5 year cases 2—survivals	18—3 year cases 5—survivals

	N_0		N_1		N_2		N_3		N_D	
	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases
5—5 year cases 2—living P_1 8—3 year cases 5—living	3 cases 1 dead 1 S.P.	5 cases 1 dead 1 S.P.	0	1 case 0 dead	1 case 1 dead 1 P.A.	1 case 1 dead 1 P.A.	1 case 1 dead 1 N.F.	1 case 1 dead 1 N.F.	0	0
7—5 year cases 2—living P_2 10—3 year cases 4—living	1 case 1 dead 1 P.F.	2 cases 1 dead 1 P.F.	1 case 0 dead	2 cases 0 dead	3 cases 2 dead 2 P+N	3 cases 2 dead 2 P+N	2 cases 2 dead 1 P.F. 1 N.F.	3 cases 3 dead 1 P.F. 1 N.F. 1 I.D.	0	0
3—5 year cases 0—living P_3 6—3 year cases 1—living	1 case 1 dead 1 P.A.	1 case 1 dead 1 P.A.	0	1 case 0 dead	1 case 1 dead 1 P.F.	1 case 1 dead 1 P.F.	1 case 1 dead 1 N.F.	3 cases 3 dead 2 N.F. 1 P+N	0	0
2—5 year cases 0—living P_4 2—3 year cases 0—living	0	0	0	0	2 cases 2 dead 1 P.F. 1 N.F.	2 cases 2 dead 1 P.F. 1 N.F.	0	0	0	0

Code: S.P.—Second Primary; P.F.—Primary Failure; P.A.—Palliative Attempt; N.F.—Node Failure; P+N—Primary plus Node Failure; I.D.—Intercurrent Disease.

TABLE VIII

CARCINOMA OF FLOOR OF MOUTH
SURVIVALS

	17 Cases with Five Year Follow-up		26 Cases with Three Year Follow-up	
No Lymph Nodes Involved	5		8	
Survivals	2	40%	5	62.5%
Primary Lesion				
<3 cm.		66⅔%		80%
>3 cm.		0%		33⅓%
Lymph Nodes Involved	12		18	
Survivals	2	16.6%	5	27.7%
All Cases	17		26	
Survivals	4	23.5%	10	38.4%

TABLE IX

CARCINOMA OF FLOOR OF MOUTH
CAUSES OF FAILURE

	17 Cases with Five Year Follow-up 13 Failures	26 Cases with Three Year Follow-up 16 Failures
Primary Failure	4	4
Lymph Node Failure—Neck	4	5
Primary plus Lymph Node Failure	2	3
Palliative Attempt	2	2
Intercurrent Disease	0	1
Second Primary	1	1

TABLE X

CARCINOMA OF GINGIVA

Over-all		No Lymph Nodes Involved		Lymph Nodes Involved	
44—5 year cases 16—survivals	69—3 year cases 30—survivals	15—5 year cases 11—survivals	27—3 year cases 20—survivals	29—5 year cases 5—survivals	42—3 year cases 8—survivals

	N_0		N_1		N_2		N_3		N_D	
	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases
6—5 year cases 5—living P_1 9—3 year cases 8—living	4 cases 0 dead	7 cases 0 dead	0	0	1 case 0 dead	1 case 0 dead	1 case 1 dead 1 N.F.	1 case 1 dead 1 N.F.	0	0
25—5 year cases 10—living P_2 41—3 year cases 20—living	8 cases 2 dead 1 P.F. 1 N.F.	16 cases 4 dead 1 P.F. 1 N.F. 2 I.D.	5 cases 4 dead 2 P+N 1 I.D. 1 O.D.	7 cases 3 dead 2 P+N 1 O.D.	5 cases 3 dead 1 N.F. 1 P+N 1 O.D.	8 cases 5 dead 2 N.F. 1 P+N 1 O.D. 1 I.F.	7 cases 6 dead 3 N.F. 3 P+N	8 cases 7 dead 4 N.F. 3 P+N	0	2 cases 2 dead 1 P+N 1 N.T.
7—5 year cases 1—living P_3 9—3 year cases 1—living	3 cases 2 dead 1 P.A. 1 I.D.	3 cases 2 dead 1 P.A. 1 I.D.	0	0	0	1 case 1 dead 1 N.F.	4 cases 4 dead 1 P.A. 2 N.F. 1 P+N	5 cases 5 dead 1 P.A. 3 N.F. 1 P+N	0	0
6—5 year cases 0—living P_4 10—3 year cases 1—living	0	2 cases 1 dead 1 N.T.	2 cases 2 dead 1 N.F. 1 P.F.	2 cases 2 dead 1 N.F. 1 P.F.	1 case 1 dead 1 N.F.	1 case 1 dead 1 N.F.	3 cases 3 dead 1 N.T. 2 N.F.	5 cases 5 dead 2 N.T. 3 N.F.	0	0

Code: I.F.—Incomplete Data; P.F.—Primary Failure; P.A.—Palliative Attempt; N.F.—Node Failure; P+N—Primary plus Node Failure; N.T.—Not Treated; I.D.—Intercurrent Disease; O.D.—Operative Death.

TABLE XI

CARCINOMA OF GINGIVA
TREATMENT

	44 Cases with Five Year Follow-up		69 Cases with Three Year Follow-up	
	16 Survivals	28 Failures	30 Survivals	39 Failures
Surgery	14	23	26	30
Radiation Therapy	1	4	2	3
Surgery plus Radiation Therapy	1	0	2	2
No Treatment	0	1	0	4

CARCINOMA OF BUCCAL MUCOSA

As indicated in Table XIV, 21 cases were available for five year study with 16 failures and 36 cases were available for three year study with 26 failures in the group of carcinoma of the buccal mucosa. Tables XV–XVII contain the pertinent data as related to this group.

CARCINOMA OF PALATE

Table XVIII includes 27 cases of carcinoma of palate qualified for five year study with 19 failures and 35 cases qualified for 3 year study with 20 failures. Tables XIX–XXI detail along identical lines the type of treatment, survivals and causes of failure in this group of cases.

TABLE XII

CARCINOMA OF GINGIVA
SURVIVALS

	44 Cases with Five Year Follow-up		69 Cases with Three Year Follow-up	
No Lymph Nodes Involved	15		27	
Survivals	11	73.3%	20	74%
Primary Lesion				
<3 cm.		100%		100%
>3 cm.		63.6%		66.6%
Lymph Nodes Involved	29		42	
Survivals	5	17.2%	8	19%
All Cases	44		69	
Survivals	16	36.3%	30	43.4%

TABLE XIII

CARCINOMA OF GINGIVA
CAUSES OF FAILURE

	44 Cases with Five Year Follow-up 28 Failures	69 Cases with Three Year Follow-up 39 Failures
Primary Failure	2	2
Lymph Node Failure—Neck	12	16
Lymph Node Failure—Distant	0	1
Primary plus Lymph Node Failure	7	8
Not Treated	1	4
Palliative Attempt	2	2
Intercurrent Disease	2	3
Operative Death	2	2
Incomplete Data	0	1

DISCUSSION OF RESULTS AND FAILURES

The results in oral cancer of all sites were, of course, much better in the group of cases in which no lymph nodes were present (Table XXII). It is discouraging to note that in the buccal mucosa series, when the neck lymph nodes were involved, there were no five year survivals. Admittedly, this is a small series and may not be significant becuase of this. Considering all cases, five year survival studies were best for lesions involving the anterior tongue.

In reviewing the failures, there were found to be 91 out of the 136 cases that qualified for a five year study (Table XXIII). Nineteen, or roughly 20 per cent of this group failed not as a result of treatment and probably should not be debited against this management program. This group of 19 were either not treated, or it was recognized at the outset that treatment would only be palliative; they died of intercurrent disease, a second primary lesion, postoperatively, or the data were incomplete. Of the remaining 71 failures, approximately

(*Text continued on page 430*)

Table XIV

CARCINOMA OF BUCCAL MUCOSA

Over-all		No Lymph Nodes Involved		Lymph Nodes Involved	
21—5 year cases 5—survivals	36—3 year cases 10—survivals	11—5 year cases 5—survivals	19—3 year cases 7—survivals	10—5 year cases 0—survivals	17—3 year cases 3—survivals

	N_0		N_1		N_2		N_3		N_D	
	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases
10—5 year cases	8 cases	10 cases	0	0	0	1 case	2 cases	3 cases	0	0
5—living	3 dead	5 dead				0 dead	2 dead	3 dead		
P_1	2 P.F.	2 P.F.								
							1 N.F.	1 N.F.		
							1 P+N	2 P+N		
14—3 year cases	1 I.F.	2 I.F.								
6—living		1 I.D.								
6—5 year cases	1 case	3 cases	0	1 case	3 cases	4 cases	2 cases	3 cases	0	0
0—living	1 dead	1 dead		1 dead	3 dead	3 dead	2 dead	3 dead		
P_2	1 P.F.	1 P.F.								
11—3 year cases				1 P+N	3 P+N	3 P+N				
3—living							2 N.F.	3 N.F.		
2—5 year cases	1 case	4 cases	0	0	1 case	2 cases	0	0	0	0
0—living	1 dead	4 dead			1 dead	1 dead				
	1 P.F.	2 P.F.								
P_3					1 N.F.					
						1 P+N				
6—3 year cases		1 O.D.								
1—living		1 I.F.								
3—5 year cases	1 case	2 cases	0	0	0	0	2 cases	3 cases	0	0
0—living	1 dead	2 dead					2 dead	3 dead		
		1 P.F.								
P_4							2 P+N	2 P+N		
5—3 year cases	1 I.D.	1 I.D.								
0—living								1 N.T.		

Code: P.F.—Primary Failure; N.T.—Not Treated; O.D.—Operative Death; N.F.—Node Failure; I.F.—Incomplete Data; P+N—Primary plus Node Failure; I.D.—Intercurrent Disease.

Table XV

CARCINOMA OF BUCCAL MUCOSA
TREATMENT

	21 Cases with Five Year Follow-up		36 Cases with Three Year Follow-up	
	5 Survivals	16 Failures	10 Survivals	26 Failures
Surgery	4	13	10	22
Radiation Therapy	1	2	0	2
Surgery plus Radiation Therapy	0	1	0	1
No Treatment	0	0	0	1

Table XVI

CARCINOMA OF BUCCAL MUCOSA
SURVIVALS

	21 Cases with Five Year Survivals		36 Cases with Three Year Survivals	
No Lymph Nodes Involved	11		19	
Survivals	5	45.4%	7	36.8%
Primary Lesion				
<3 cm.		62.5%		50%
>3 cm.		0%		22.2%
Lymph Nodes Involved	10		17	
Survivals	0	0%	3	17.6%
All Cases	21		36	
Survivals	5	23.3%	10	27.7%

TABLE XVII

CARCINOMA OF BUCCAL MUCOSA
CAUSES OF FAILURE

	21 Cases with Five Year Follow-up 16 Failures	36 Cases with Three Year Follow-up 26 Failures
Primary Failure	4	6
Lymph Node Failure—Neck	4	4
Primary plus Lymph Node Failure	6	9
Intercurrent Disease	1	2
Incomplete Data	1	3
Not Treated	0	1
Operative Death	0	1

TABLE XIX

CARCINOMA OF PALATE
TREATMENT

	27 Cases with Five Year Follow-up		35 Cases with Three Year Follow-up	
	8 Survivals	19 Failures	15 Survivals	20 Failures
Surgery	5	3	8	4
Radiation Therapy	2	10	4	10
Surgery plus Radiation Therapy	1	5	3	4
No Treatment	0	1	0	2

TABLE XVIII

CARCINOMA OF PALATE

Over-all		No Lymph Nodes Involved		Lymph Nodes Involved	
27—5 year cases 8—survivals	35—3 year cases 15—survivals	15—5 year cases 7—survivals	20—3 year cases 13—survivals	12—5 year cases 1—survivals	15—3 year cases 2—survivals

	N_0		N_1		N_2		N_3		N_D	
	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases	5 year cases	3 year cases
7—5 year cases 6—living P_1 10—3 year cases 9—living	6 cases 1 dead 1 S.P.	9 cases 1 dead 1 N.T.	0	0	1 case 0 dead	1 case 0 dead	0	0	0	0
14—5 year cases 1—living P_2 15—3 year cases 3—living	7 cases 6 dead 6 P.F.	8 cases 5 dead 5 P.F.	1 case 1 dead 1 N.T.	1 case 1 dead 1 N.T.	2 cases 2 dead 2 N.F.	2 cases 2 dead 2 N.F.	4 cases 4 dead 4 N.F.	4 cases 4 dead 4 N.F.	0	0
4—5 year cases 1—living P_3 5—3 year cases 3—living	1 case 0 dead	2 cases 0 dead	0	0	0	0	3 cases 3 dead 1 N.F. 1 P.A. 1 P+N	3 cases 2 dead 1 N.F. 1 P.A.	0	0
2—5 year cases 0—living P_4 5—3 year cases 0—living	1 case 1 dead 1 P+N	1 case 1 dead 1 P.A.	0	0	0	1 case 1 dead 1 P+N	1 case 1 dead 1 P.A.	3 cases 3 dead 2 P.A. 1 N.F.	0	0

Code: P.F.—Primary Failure; N.F.—Node Failure; S.P.—Second Primary; N.T.—Not Treated; P.A.—Palliative Attempt; P+N—Primary plus Node Failure.

TABLE XX

CARCINOMA OF PALATE
SURVIVALS

	27 Cases with Five Year Follow-up		35 Cases with Three Year Follow-up	
No Lymph Nodes Involved	15		20	
Survivals	7	46.6%	13	65%
Primary Lesion				
<3 cm.		83.3%		88.8%
>3 cm.		11.1%		45.4%
Lymph Nodes Involved	12		15	
Survivals	1	8.3%	2	13.3%
All Cases	27		35	
Survivals	8	29.6%	15	42.8%

TABLE XXI

CARCINOMA OF PALATE
CAUSES OF FAILURE

	27 Cases with Five Year Follow-up 19 Failures	35 Cases with Three Year Follow-up 20 Failures
Primary Failure	6	5
Lymph Node Failure—Neck	7	8
Primary plus Lymph Node Failure	2	2
Not Treated	1	2
Palliative Attempt	2	3
Second Primary	1	0

TABLE XXIII

ORAL CANCER
CAUSES OF FAILURE

	136 Cases with Five Year Follow-up 91 Failures	218 Cases with Three Year Follow-up 127 Failures
Primary Failure	17	19
Lymph Node Failure—Neck	34	46
Lymph Node Failure—Distant	1	2
Primary plus Lymph Node Failure	20	27
Not Treated	3	10
Palliative Attempt	8	9
Intercurrent Disease	3	6
Second Primary	2	1
Operative Death	2	3
Incomplete Data	1	4

one-fourth were due to lack of control of the primary lesion and approximately three-fourths to uncontrolled metastatic lesions. Roughly, this same ratio carried through the three year studies, even though this series of cases was larger. As can be seen from Table 1, surgery was used in proportion more frequently in the group of cases that survived than in those that failed. The ratio was twice as high in the group of failures than in the group of survivals. This is naturally so since, as was stated earlier, radiation therapy was employed when surgical removal could not be done, and, accordingly, was used in the more advanced cases (Table XXIV).

TABLE XXII

ORAL CANCER
PERCENTAGE SURVIVAL RATES

136 Cases with Five Year Follow-up 218 Cases with Three Year Follow-up

	Anterior Tongue		Floor of Mouth		Gingiva		Buccal Mucosa		Palate	
	27—5 Year Cases	52—3 Year Cases	17—5 Year Cases	26—3 Year Cases	44—5 Year Cases	69—3 Year Cases	21—5 Year Cases	36—3 Year Cases	27—5 Year Cases	35—3 Year Cases
No Lymph Nodes Involved	90.0	83.3	40.0	62.5	73.3	74.0	45.4	36.8	46.6	65
Lymph Nodes Involved	17.6	21.4	16.6	27.7	17.2	19.0	0	17.6	8.3	13.3
All Cases	44.4	50.0	23.5	38.4	36.3	43.4	23.3	27.7	29.6	42.8

TABLE XXIV

ORAL CANCER
EXTENT OF DISEASE

	136 Cases with Five Year Follow-up				218 Cases with Three Year Follow-up					
	N_0		N_1		N_2		N_3		N_D	
	5	3	5	3	5	3	5	3	5	3
P_1	31	51	1	4	5	7	8	9	0	0
P_2	17	32	7	11	16	22	19	25	1	3
P_3	6	10	0	1	2	4	9	13	0	0
P_4	2	6	2	2	3	5	7	13	0	0

One difficulty in comparing results in different series of cases may be a disproportionate number of favorable or unfavorable cases in one, as compared with another. It would be helpful, therefore, to know the percentage of the various types of involvement.

Grouping the 136 five year exposure cases according to the extent of the primary lesion and lymph node involvement (Table XXIV) we have: P_1, 45 or 33.1 per cent; P_2, 60 or 44.1 per cent; P_3, 17 or 12.5 per cent; P_4, 14 or 10.3 per cent; N_0, 56 or 41.2 per cent; N_1, 10 or 7.3 per cent; N_2, 26 or 19.1 per cent; N_3, 43 or 31.6 per cent; N_D, 1 or 0.7 per cent.

If a series had a much higher percentage of more favorable cases, the end results should be better; if the reverse were true, the end results, of course, would be lower.

CONCLUSIONS

1. An analysis was made of 136 cases of head and neck cancer, five or more years, and 218 cases, three or more years after treatment.

2. The results were better in the group of cases that presented no metastases.

3. Most of the failures were due to lack of control of the metastatic lesions.

Department of Surgery
Ohio State University Health Center
Columbus, Ohio

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SPACE DOSE RELATIONSHIPS FOR POINTS A AND B IN THE RADIUM THERAPY OF CANCER OF THE UTERINE CERVIX*

By GEORGE C. LEWIS, Jr., M.D., ANTOLIN RAVENTOS, M.D., *and* JOHN HALE, Ph.D.
PHILADELPHIA, PENNSYLVANIA

DURING the course of a study of radium dosimetry in the therapy of uterine cervical cancer, it became apparent that the positions of the reference points A and B,[5,7,8,9] frequently used for parametrial and lateral pelvic wall dosage control, were subject to many variations. Therefore, the location of these points relative to the bony pelvis was accurately established for each of a group of patients. It was found that the variations were frequently significant. It is the purpose of this paper to present the range in location of points A and B and to examine the clinical data for factors which might influence them. The actual dose rates of points A and B are determined and contrasted with those which would be expected if there were no such clinical variations.

MATERIALS AND METHODS

During the period from April, 1952, to June, 1956, orthographic roentgenography[3] was used to control dosage for all of the 166 patients treated with radium at the Hospital of the University of Pennsylvania for malignancy involving the uterine cervix. Twenty patients were excluded from this analysis because of a total or supravaginal hysterectomy prior to irradiation or because the bony pelvis was inadequately demonstrated on the roentgenograms. There were 156 applications of radium in the remaining 146 patients.

The age and parity distribution for the 146 patients is given in Tables I and II. Four of the patients had adenocarcinoma involving the corpus and cervix. Since primary sites could not be determined, they were classified as carcinoma corporis et colli. The remaining patients had primary cervical malignancy: 136 squamous cell carcinoma, 2 adenocarcinoma, 3 adenoacanthoma, and 1 both squamous cell and adenocarcinoma. The International Stage of these patients is shown in Table III. The frequency of clinical involvement of various

Table I

NUMBER OF PATIENTS ACCORDING TO AGE, BY DECADES

Age	No.
20–29	5
30–39	26
40–49	41
50–59	39
60–69	20
70-plus	15
Total	146

Table II

NUMBER OF PATIENTS ACCORDING TO PARITY

Parity	No.
0	26
I	32
II	33
III	14
IV	13
V plus	28
Total	146

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From the Department of Obstetrics and Gynecology and the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania.

Table III

INTERNATIONAL STAGE OF 142 PATIENTS WITH PRIMARY CERVICAL CANCER

Stage	No.
O	2
I	62
II	53
III	18
IV	3
V	4
Total	142

local sites by cancer which had spread beyond the cervix is given in Table IV.

The Ernst applicator[1] and the Manchester applicators as modified by Hankins and Hockin[2] were the only radium containers that were utilized (Table V). In the cases for which the Manchester applicators were employed, the choice of the size of the ovoids and spacer was based upon the size of the vaginal vault. Table VI indicates the number of insertions that occurred on the basis of the combined transverse widths of the two ovoids and spacer utilized for each insertion. Containers were classed as rigid when the component parts were firmly interlocked, and non-rigid when the parts were loosely related to one another. The Ernst applicator was classed as rigid. The first 38 Manchester type insertions were non-rigid. In order to obtain a rigid system, the instrument was altered by the use of a metal intrauterine stem which could be firmly attached to the spacer (Fig. 1). Despite this, in 11 cases, there was a displacement of the spacer or ovoid. These cases were included in the study of non-rigid containers.

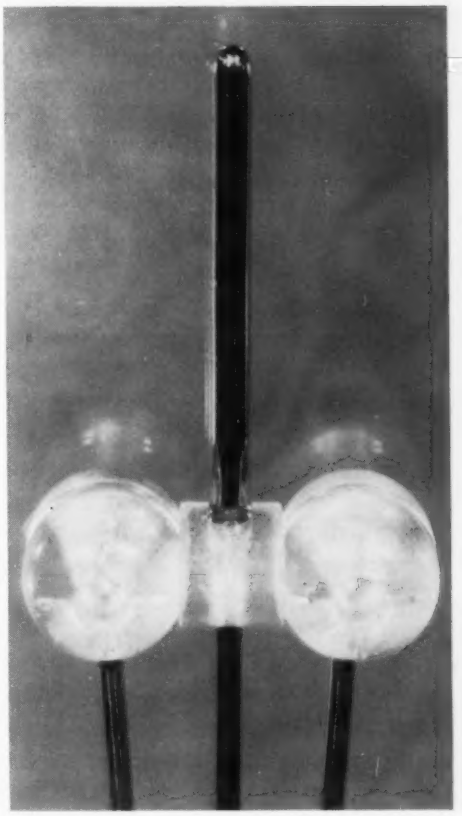

Fig. 1. Manchester type applicator of Hankins and Hockin modified by rigid metallic stem secured in spacer.

Prior to the application of radium, radiopaque catheters were placed in the ureters.

Table IV

FREQUENCY OF CLINICAL INVOLVEMENT BY CANCER OF SITES BEYOND THE CERVIX

Site	No. Involved
Rectovaginal septum	16
Vesicovaginal septum	27
Lateral fornix	11
Right parametrium, partial	30
Left parametrium, partial	25
Right parametrium, complete	13
Left parametrium, complete	19
Endometrium	12
Beyond above sites	5

Table V

FREQUENCY OF INSERTIONS OF ERNST AND MANCHESTER TYPE RADIUM CONTAINERS FOR THE 156 APPLICATIONS

Type	No.
Ernst	25
Manchester—non-rigid	38
Manchester—rigid intact	82
displaced	11
Total applications	156

TABLE VI

NUMBER OF RADIUM INSERTIONS, MANCHESTER TYPE, ON BASIS OF THE COMBINED TRANSVERSE WIDTH OF SPACER AND OVOIDS

Transverse Width	No. of Insertions
3.0 cm.	30
3.5 cm.	37
4.0 cm.	41
4.5 cm.	23

Two hundred ninety seven ureters were catheterized. The radium was insterted and 7 roentgenograms were made, following the technique of orthographic roentgenography previously described.[3] Roentgenographic distortion was eliminated by the use of a pantograph which produced the true scale images of the radium containers, the ureteral catheters, the bony pelvis, the bladder, and the rectum. For the purpose of this paper, only the relations of the bony pelvis, radium, and the ureters are considered.

The spatial and dosage relationships of the reference points A and B of Tod and Meredith[7] were studied, using two entirely different approaches for each patient.

1. A precalculated dose rate was obtained at points A and B. These precalculated values were based upon locations of the points on paper relative to an idealized position of the uterus and vaginal fornices as described by Tod and Meredith[7] in 1938 (Fig. 2). As recommended by these authors, calculations were based upon the type of applicator and the radium loading that was employed in the patient, but no reference was made to the roentgenograms.

2. The actual locations of points A and B in the pelvis were determined on the basis of the roentgenograms. The details of this procedure are given in the appendix of this paper. In keeping with the definitions of Tod and Meredith[5,7,8,9] and following a personal communication from Meredith,[6] it was decided to locate point A as the center of a sphere of 2 cm. radius, the surface of which was tangent to a fornix at

FIG. 2. Ideal arrangement of points A and B as portrayed by Tod and Meredith in 1938. (Reproduced by permission from the authors and *The British Journal of Radiology*.)

the most superior surface and to the long axis of the uterus. The surface of the vaginal radium container was used to define the fornix. Point B was also located 2 cm. superior to the fornix, but the measurement was taken along a line parallel to the mid-sagittal pelvic plane. Point B was placed 5 cm. from the mid-sagittal plane. Both point A and point B were lateral to the uterus and in the plane of the uterus.

In order to specify locations of points A and B relative to the bony pelvis, three planes of reference and a line between the superior margins of the acetabula (the interacetabular line) were used. The planes were: (1) the mid-sagittal plane; (2) the transverse plane perpendicular to the roentgenographic table and containing the interacetabular line; and (3) the coronal plane perpendicular to the mid-sagittal and transverse planes passing through the same line. The steps involved in establishing the spatial relationships of points A and B to the bony pelvis are detailed in the appendix. These relationships are:

1. Left and right relationships of point A with respect to the mid-sagittal plane.

2. Superior and inferior measurements of points A and B relative to the transverse plane.

3. Anterior and posterior relationships of

points A and B with respect to the coronal plane.

4. The distance from point B to the lateral pelvic wall at its closest point. The inner aspect of the lateral bony wall was defined by a line passing along the iliopectineal line with a projection to terminate at the lateral margin of the obturator foramen.

The exposure dose rates in r/hr. for both points were determined by the position of the points with respect to each radium container. These determinations were called "actual values." In the results presented herewith the dose rates are expressed as ratios of actual to precalculated values and as ratios of left actual values to right actual values.

All data regarding the clinical observations, spatial relationships, and dose rates were transferred to business machine cards. The distribution and relationships of results were obtained by machine card selection and correlation. The relations were tested for significance by standard statistical methods.

RESULTS

The locations of points A and B relative to the planes established within the bony pelvis showed marked variation. The data with regard to mean value, standard deviation, and significant difference for the entire group are summarized in Table VII for point A. The values for point B for similar observations relative to coronal and transverse planes were nearly identical to those of point A and are therefore not included in the table. The values and standard deviations for right point A were essentially the same as the left point A data given in the table.

The locations of points A and B with regard to the transverse plane varied from 2.5 cm. inferior to 5.5 cm. superior. They were also found to vary from 2.0 cm. anterior to 4.5 cm. posterior to the coronal plane. The maximum point A to sagittal plane distance was 4.5 cm. In two cases point A was found to be 0.5 cm. from the sagittal plane on the opposite side of the pelvis from its anticipated location.

The apparent influence of the clinical factors on point B location was almost identical to that observed for point A. For this reason the influence of clinical factors upon point B location is summarized for point A alone in Table VII.

Parity was noted to have no significant effect on any of the locations of points A and B relative to the planes. The distance from point A to the sagittal plane was not influenced by any of the clinical factors. The distance from point A to point B was found to be related to the displacement of point A from the mid-sagittal plane, as might be expected.

The relationship of points A and B to the transverse and coronal planes was found to be significantly correlated with age, type of radium applicator, and stage of disease (Table VII). For the older patients or those whose disease was advanced, points A and B were more posterior and inferior. Points A and B were relatively posterior and inferior for the Ernst and smallest Manchester applicator. For the larger Manchester ovoids points A and B were noted to be progressively more anterior and superior in location.

The locations of both point A and point B seemed to vary in the same manner in accordance with the stage of the disease and the apparent degree of parametrial involvement. In cases of more advanced disease, points A and B were located more posterior and inferior than for involvement of the cervix alone.

The shortest distance from point A to the ureter was found to vary markedly. The mean value for this distance was 1.95 $\pm$0.90 cm. The greatest value for this distance was 4.5 cm. In 1 per cent of the measurements point A was less than 0.3 cm. from a ureter, and in 7 per cent point A was less than 0.8 cm. from a ureter. The relationship of point A to the ureter was studied relative to the exposure dose rate the ureter received nearest point A. Point A was nearest a relatively low dose rate sec-

TABLE VII

LOCATION OF LEFT POINT A WITH RELATION TO TRANSVERSE, CORONAL AND SAGITTAL PLANES*

Clinical Observation		Statistical Observation								
		Transverse Plane			Coronal Plane			Sagittal Plane		
		Mean	±S.D.†	p= <‡	Mean	±S.D.†	p= <‡	Mean	±S.D.†	p= <‡
Entire Group		+0.80	1.4		−1.30	1.2		1.95	0.80	
Age	20–39	+2.00	1.6	.01	−0.50	1.00	.001	1.90	0.88	
	40–59	+0.63	1.2	.01	−1.32	1.30	.01	1.95	0.63	
	60+	−0.05	0.96		−1.95	0.95		2.05	0.91	
Stage	O+I	+1.45	1.53	.001 .001	−0.85	0.93	.01	1.95	0.81	
	II	+0.40	1.0		−1.35	1.10	.001	1.95	0.84	
	III+IV	0.00	1.1		−1.95	1.30		2.00	0.84	
Site§ Involved	a	+1.45	1.53	.01	−0.85	0.94		1.95	0.81	
	b	+0.55	0.93	.001 .001	−1.15	1.05	.001	1.80	0.96	
	c	+1.10	1.18		−1.50	1.09		2.20	0.53	
	d	0.00	1.07		−1.90	1.04		1.80	0.95	
Ernst Applic.		+0.15	0.82		−2.40	0.95	.001	2.30	0.70	
Type of Manchester Applic.‖	3.0	+0.10	1.1	.05 .001	−1.35	0.92		1.85	0.85	
	3.5	+0.45	1.1		−1.30	0.90		1.90	0.70	
	4.0	+0.85	1.6		−1.30	1.20	.001	2.00	0.90	
	4.5	+2.65	1.7		−0.10	1.10		1.85	0.80	
Parity	0	+0.65	0.94		−1.35	0.96		1.95	0.94	
	1	+0.70	1.2		−1.55	1.40		2.00	0.87	
	2	+0.65	1.3		−1.05	1.30		2.10	0.82	
	3+4	+1.35	1.7		−0.95	1.30		1.75	0.84	
	5+	+0.50	1.7		−1.55	1.10		1.95	0.71	

* Values superior to transverse plane or anterior to coronal plane designated as +; inferior or posterior values as −.
† Standard deviation of single values.
‡ p designated for significant differences. Differences not indicated were tested and were found not significant.
§ Site involved by tumor clinically: (a) cervix alone, or with endometrium or with distant metastasis; (b) vaginal extension; (c) one side of parametrium; (d) both sides of parametrium.
‖ Manchester applicator arranged according to transverse width of vaginal components in centimeters.

tion of the ureter 87 times, an intermediate dose rate section 51 times, and a high dose rate section 159 times.

The mean distance from point B to the lateral pelvic wall was 1.05 ±0.82 cm. Its location varied from 3 cm. medial to 1.5 cm. lateral to the internal pelvic wall surface. No correlation was found between the relationship of point B to the pelvic wall and the clinical factors.

It was found that for the non-rigid vaginal applicator the uterus was relatively anteverted. For the Ernst applicator the long uterine axis was found to be on the average almost parallel to the coronal plane. For the rigid Manchester applicator the uterine position was intermediate between these extremes (Fig. 3). The mean

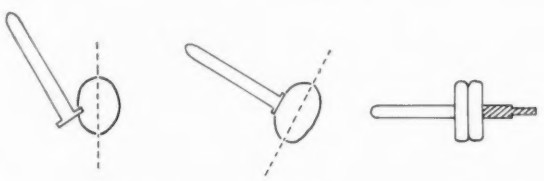

FIG. 3. Lateral view of non-rigid and rigid Manchester applicators and the Ernst applicator showing the average relative position of the intrauterine stem within the pelvis.

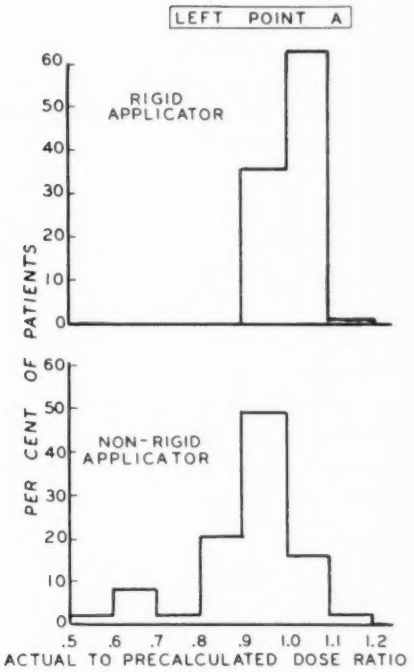

FIG. 4. Distribution of cases according to ratio of actual to precalculated exposure dose at left point A for rigid and non-rigid radium containers.

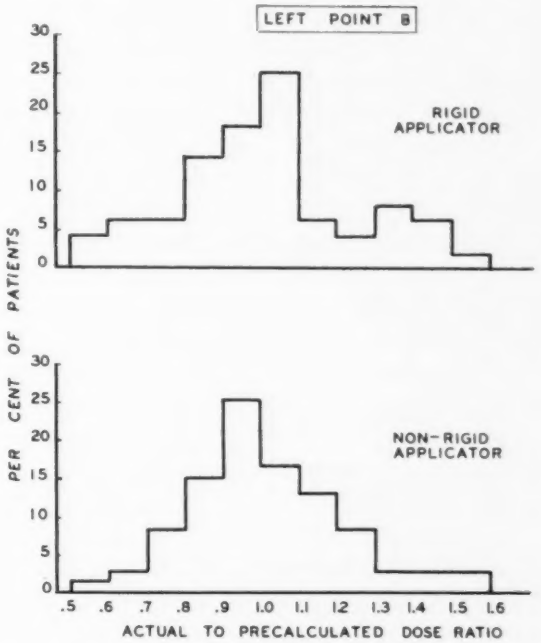

FIG. 5. Distribution of cases according to ratio of actual to precalculated exposure dose at left point B for rigid and non-rigid radium containers.

value for the angle between coronal plane and uterine axis was found to be 21.2°, −2.1°, and 9.8°, respectively, for these different types of applicators.

Left and right point A were at nearly the same level relative to the transverse plane in 83 cases. In 45 cases point A on the right was more than 0.5 cm. superior to point A on the left. In 28 cases left point A was more than 0.5 cm. superior. The maximum difference was 2.5 cm.

For point A, the ratio of actual to precalculated exposure dose approximated the 1.0 for the rigid applicator, but the ratio varied widely for the non-rigid applicator (Fig. 4).

In contrast the ratios for point B did not exhibit this dependence upon the type of container. Rigid and non-rigid containers alike were associated with wide variations in the ratio of actual to precalculated exposure dose rates (Fig. 5).

The ratio of actual left point A exposure dose to actual right point A exposure dose is presented in Figure 6. It is apparent that

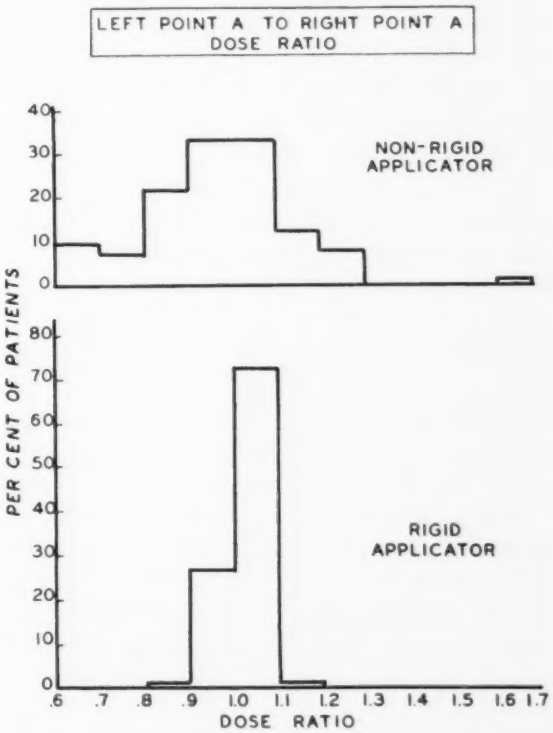

FIG. 6. Distribution of cases according to the ratio of actual left point A exposure dose to actual right point A exposure dose for rigid and non-rigid radium containers.

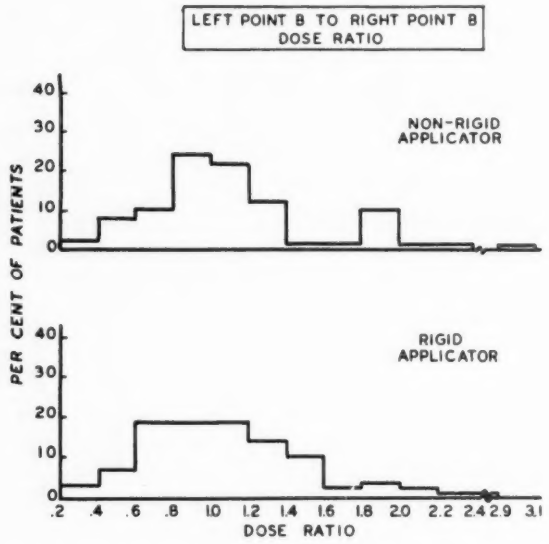

FIG. 7. Distribution of cases according to the ratio of actual left point B exposure dose to actual right point B exposure dose for rigid and non-rigid radium containers.

the ratio approached unity for rigid containers but varied widely for non-rigid applicators. Corresponding ratios for point B are shown in Figure 7. There is a wide variation in the ratios observed regardless of the type of applicator.

DISCUSSION

Several systems have been proposed for the estimation of exposure dose from radium to tumor and vital pelvic organs during the treatment of uterine cervical cancer.[4] One of the most notable advances in the control of radium therapy was the method of expressing the dose at two specific points in the pelvis first described by Tod and Meredith in 1938.[7] These points have been widely used to represent the dosage pattern about an applicator which contains a specifically distributed quantity of radium. The definition of the locations of the points by Tod and Meredith is based upon several anatomic structures within the pelvis. The vaginal fornix and the mid-uterine axis serve to locate point A. The fornix and the mid-sagittal plane of the pelvis are utilized to locate point B. Point A was considered to be close to the junction of the ureter and uterine artery. Point B was thought to be in the region of the obturator lymph nodes.

The points have come into use without reference to anatomic variations of each patient or to the position of the applicator as actually accomplished in the patient. In some cases pelvic structures may be distorted by the tumor or allied pelvic disease. When a radium applicator does not have rigidly interlocked parts, it is possible that the final position of the segments in the patient may vary greatly from the planned pattern. These variations in anatomy or applicator arrangement may result in marked alterations of exposure dose rates from those calculated for an idealized application. In addition, the definitions of the points' locations do not refer to their positions within the bony pelvis except in relation to the mid-sagittal plane. Since radium therapy is frequently used in conjunction with external beam therapy, the correlation of these modalities would be aided greatly by a further knowledge of the locations of the points within the bony pelvis.

Meredith, in his personal communication,[6] stated: "The calculation of dosage at point A was carried out on ideal arrangements but it was soon realized that (a) these were seldom achieved in practice and (b) that from radiographs it was often not possible to determine the level of the fornices upon which the original definition depends. The latter might be because the ovoid outline was not visible in the radiograph, or the ovoids were pushed out because the tumor filled the fornix, or for other reasons." In 1953 Tod and Meredith[9] tried to avoid some of these problems by using the lower end of the intrauterine radium to establish the level of the fornices. In this study, the modification proposed by Tod and Meredith in 1953 was not employed because the vaginal fornix was identified in all cases and because, despite the modifications, the use of a non-rigid applicator could still result in variations in the actual exposure dose from the precalculated values.

The use of orthographic pelvimetry has

permitted a detailed study of the actual locations of points A and B for 156 applications. When the entire group of applications is considered in terms of mean values for the locations of points A and B, an "average" picture can be visualized. Point A is slightly superior and posterior to the interacetabular line and 2 cm. from the midsagittal plane. Point B is at the same level but 1 cm. from the lateral pelvic wall. It is to be remembered that points A and B were found to vary as much as 8 cm. in the superior-inferior direction and 6.5 cm. in the anteroposterior direction, and that in 2 cases point A was found to be on a side opposite its anticipated location. Indeed the wide variations in the positions of points A and B encountered in this study make it apparent that the "average" picture cannot be used in the individual case in lieu of roentgenographic localization of points A and B.

The concept that point A is close to the ureter was not borne out by this study. In 93 per cent of the observations the distance from ureter to point A was 0.8 cm. or greater. The portion of the ureter receiving the highest dose rate was nearest point A in only 53 per cent of the cases. It would appear that point A is not a good indicator for the location of the ureter, and that the point on the ureter nearest point A is not representative of the maximum ureteral dose. Accurate estimations of the ureteral exposure dose rate require determination of the ureter location in relation to the source of radiation.

Age appears to influence the location of points A and B. The youngest patients have a mean value for point A and point B location more superior and anterior than the mean value for older groups of patients. This may be related to the greater pliability of tissues in the younger patients which will permit a greater degree of displacement of vaginal vault and uterus by the intravaginal packing which supports the radium container.

Similarly, the stage of disease may influence the location of points A and B by altering the paracervical and paravaginal tissues' pliability. They observed more posterior and inferior mean values for the location of these points in cases with advanced disease probably reflects the result of tissue infiltration, displacement, and fixation by tumor, with an associated pelvic cellulitis.

The observed positions of points A and B were related to the size and type of applicator. In the applicators defined here as rigid, the vaginal and intrauterine components are interlocked in such a manner that a consistent and symmetric relationship of uterus and vaginal fornices is usually attained. The Ernst applicator, in addition to being rigid, has a stem within the vagina which tends to influence its position.

The non-rigid applicator permitted the central uterine axis to be more anterior and superior in position. The loose relationship of the applicator segments apparently allows a greater displacement of the pelvic structures by the vaginal packing. The rigid applicator tended to align the uterus with the vagina in such a way that the central uterine axis was not as far anterior or superior as for the non-rigid applicator. The intravaginal stem of the Ernst applicator, surrounded by packing, tended to hold the applicator in the position in which it was inserted, *i.e.*, almost parallel to the operating table (patient in the lithotomy position).

For the Manchester type of insertions, the largest size of vaginal components which could be inserted were used. The patients with the most capacious vaginas received the largest applicators. In these cases the more pliable tissues permitted points A and B to be much more anterior and superior than for patients who had small vaginas. Usually the Ernst applicator with only four of its vaginal containers was employed in those patients whose vaginas were too small for even the smallest Manchester ovoid-spacer combinations. This limitation on the use of the Ernst applicator in addition to factors already cited provides an explanation for the more posterior and inferior location of points A and B associated with the applicator.

The most important observations were those concerning the exposure dose rates. Precalculated exposure dose rates were unreliable for point A estimates when non-rigid applicators were used, and unreliable for point B estimates regardless of the type of applicator.

It is to be expected that rigid applicators should be associated with a consistent correlation of precalculated to actual exposure dose rate at point A, since for practical purposes the location of points A (left and right) is defined relative to the radium. For the rigid applicator the segments of the instrument maintain the same inter-relationship in the patient as that utilized in determining the precalculated exposure dose rate. The discrepancy observed for exposure dose rate at point A with non-rigid applicators must be attributed to the fact that the radium inter-relationship in the patient is not necessarily that upon which the precalculated determination was based.

The differences in precalculated and actual exposure dose rates at point B regardless of the type of applicator are essentially due to the fact that the precalculation of point B exposure rate is based upon an assumed symmetric arrangement of uterus and vagina with reference to the mid-sagittal plane. In the course of the actual application of radium, these same structures will frequently attain asymmetric relationships to the mid-sagittal plane. For this reason, and the fact that point B is defined at a fixed distance from the mid-sagittal plane, it must be expected that point B dose rates in such patients will vary with relation to precalculated values and with relation to the contralateral point B.

SUMMARY AND CONCLUSION

Points A and B of Tod and Meredith were located with reference to the bony pelvis and genital structures in 156 applications of radium for malignancy involving the cervix in 146 patients between 1952 and 1956. Orthographic roentgenography provided an accurate means for the determination of the points' locations in these patients.

The "average" location of point A was found to be slightly superior and posterior to the superior aspects of the acetabula, and 2 cm. from the mid-sagittal plane. The "average" location of point B was at the same level but 1 cm. from the lateral pelvic wall. Great variations from these average locations were encountered in individual cases. Points A and B were more posterior and inferior in older patients, patients with advanced disease, and patients whose vaginal size required the use of smaller applicators. None of these factors appeared to influence the relationship of point A to the mid-sagittal plane or the distance of point B from the lateral pelvic wall. Parity was not found to be correlated with either point's location. The location of point A did not reliably represent ureteral position nor was it consistently near the portion of the ureter which received the highest exposure dose rate.

Rigid applicators were associated with a more posterior and inferior location of points A and B than the non-rigid containers. The most posterior and inferior locations of points A and B were observed with the Ernst applicator.

Precalculated exposure dose rates (calculated without reference to the individual patient's roentgenograms) were a reliable estimate of actual values at point A, when rigid applicators were used. When non-rigid applicators were employed, no reliable relationship was noted. For point B, precalculated values did not consistently represent the actual values regardless of the type of applicator used.

The very wide discrepancies between "precalculated" and actual exposure dose rates for points A and B indicate that the routine use of tissue dose estimates which are based on hypothetical arrangements of the radium may frequently lead to substantial errors. Furthermore, the individual variations in the locations of the points suggest that it may be a fallacy to assume that any points defined in relation to the

radium are consistently representative of the location of any anatomic structure other than the uterus and vagina. Therefore, it is felt that the application of radium for cervical cancer should be followed immediately by roentgenographic evaluation of the container's position. An estimate should be made of the actual dose rates for the vital structures of the individual pelvis. This can be done by using roentgenographic procedures such as the one described, with appropriate contrast media for visualization of the rectum and urinary tract. Some therapists prefer to use a probe dosimeter or other measuring device instead of contrast medium localization to supplement the roentgenographic evaluation of the applicator position. Though there has been no experience with these devices in the series reported herewith, it appears that in principle they should be satisfactory. Following dosage estimation, the exposure dosage for tumor bearing areas can be regulated to attain desired treatment levels by altering the radium loading, time of exposure, or subsequent therapy, with due regard for the tolerance of the contiguous vital structures.

APPENDIX

DETERMINATION OF SPATIAL RELATIONSHIPS OF POINTS A AND B WITH REFERENCE TO THE BONY PELVIS

The spatial relationships of points A and B are established by the use of the reference structures and plane described by Tod and Meredith[7] as well as several bony structures which are readily visualized in the anteroposterior and lateral roentgenograms of the pelvis. Figures 8 to 17 depict steps that are followed in a case to establish the relationships of points A and B. In order to demonstrate more clearly several of the steps, the left acetabulum is depicted more superior and anterior to the right acetabulum than it was observed in any of the patients studied. When the procedure outlined is followed for an individual patient, it must be remembered that some of the anterior, superior, or lateral relationships shown in the figures may be reversed.

Determination of the locations of points A and B requires the use of a specially constructed roentgenographic table so as to produce anteroposterior and lateral roentgenograms that are exactly perpendicular to each other (orthographic). The construction of the table permits an accurate knowledge of the course of the anteroposterior and lateral roentgenographic beams through the pelvis. From this knowledge precise measurements are made within the patient. Distortion of roentgenographic images due to roentgen-ray beam divergence is corrected by a pantograph which allows images to be drawn in their true dimensions.[3]

The pantograph is used to prepare a true

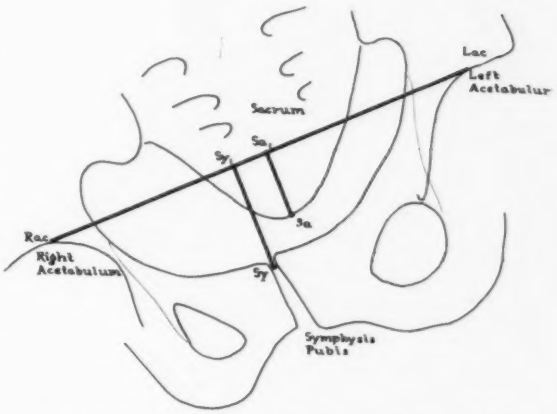

Fig. 8. Anteroposterior drawing of the pelvis.

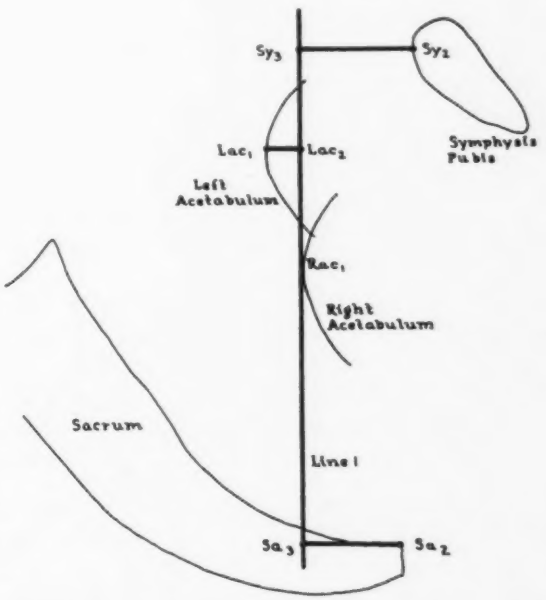

Fig. 9. Lateral drawing of the pelvis.

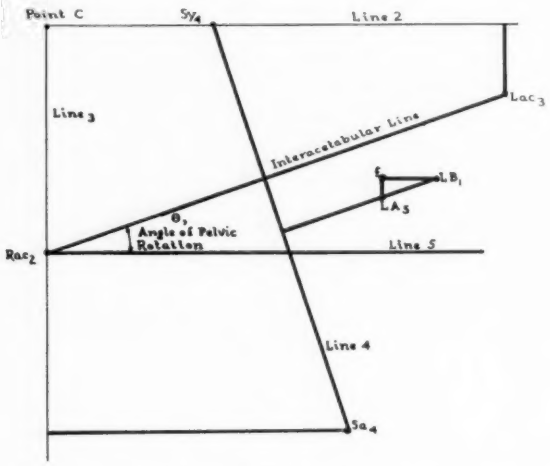

FIG. 10. Transverse plane drawing of the pelvis.

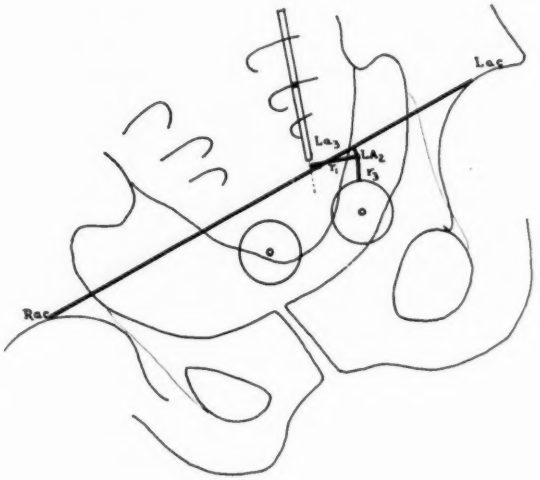

FIG. 12. Anteroposterior drawing of the pelvis.

size drawing in the anteroposterior and lateral views. For this study, the two drawings included the images of the following: (1) radium containers; (2) ureteral catheters; (3) bony pelvis: (a) symphysis pubis, (b) acetabula, (c) anterior surface of the sacrum in the midsagittal plane from the sacral promontory to the sacrococcygeal joint or the most inferior point of the sacrum which could be visualized, and (d) lateral pelvic wall, medial surface, as determined on the anteroposterior roentgenogram from the sacroiliac joint along the iliopectineal line to the lateral margin of the obturator foramen.

The anteroposterior and lateral drawings are used to prepare a transverse plane drawing upon which are projected several of the points of interest. This drawing is in a plane perpendicular to the anteroposterior drawing and contains the most superior points of each acetabulum. The following steps are utilized to establish image locations on the transverse drawing:

1. As indicated in the anteroposterior drawing (Fig. 8), lines Rac-Lac, Sa-Sa_1 and Sy-Sy_1 are established utilizing the bony images. Lines Sa-Sa_1 and Sy-Sy_1 are perpendicular to line Rac-Lac.

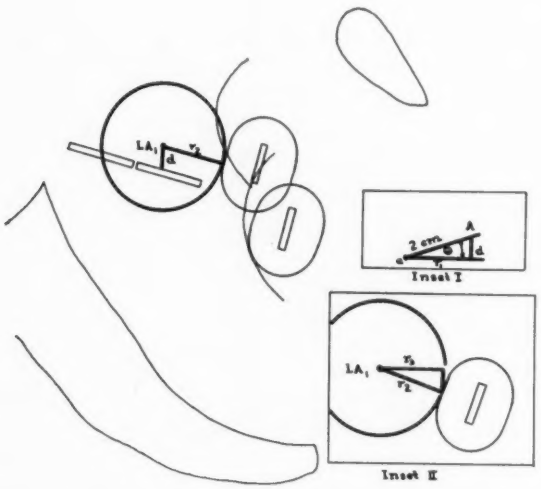

FIG. 11. Lateral drawing of the pelvis.

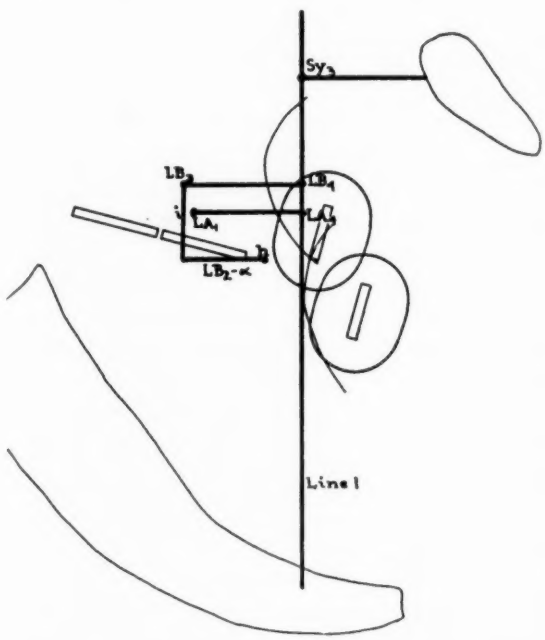

FIG. 13. Lateral drawing of the pelvis.

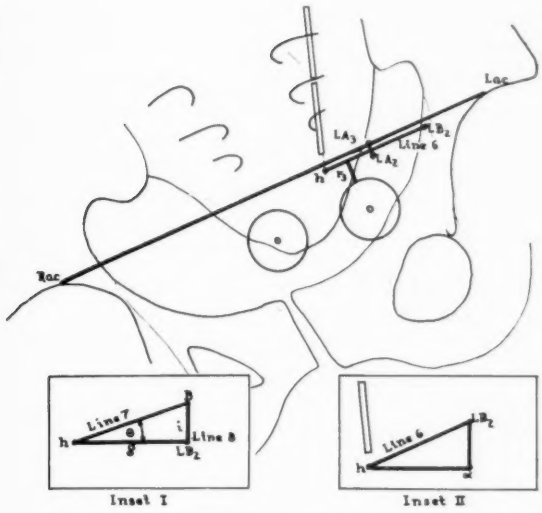

Fig. 14. Anteroposterior drawing of the pelvis.

2. The images of the lateral drawing (Fig. 9) are utilized to provide anteroposterior relationships. Line 1 is drawn perpendicular to the plane of the anteroposterior drawing and tangent to the superior aspect of the right acetabulum at point Rac_1. Lines Sy_2-Sy_3, Sa_2-Sa_3 and Lac_1-Lac_2 are drawn perpendicular to line 1.

3. The transverse drawing (Fig. 10) is obtained by reference to measurements established in the drawings of Figures 8 and 9. Two perpendicular lines, 2 and 3, are drawn so as to intersect at an arbitrary point c—in the left upper corner of the drawing. Point Sy_4 is established by measuring along line 2 from point c the distance Rac-Sy_1 (Fig. 8). Point Rac_2 is located by measuring the distance Sy_3-Rac_1 (Fig. 9) from point c along line 3. Point Lac_3 is located by the use of distances Rac-Lac (Fig. 8) and Sy_3-Lac_2 (Fig. 9) measured horizontally and vertically respectively from point c. Sa_4 is established in the same manner using measurements Rac-Sa_1 (Fig. 8) and Sy_3-Sa_3 (Fig. 9). Rac_2 and Lac_3 are connected by a line (the interacetabular line). Sy_4 and Sa_4 are connected by line 4. This line represents the intersection of the plane of the drawing with the mid-sagittal plane of the pelvis.

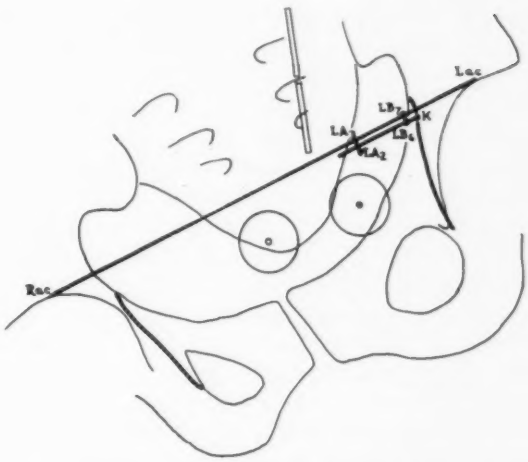

Fig. 16. Anteroposterior drawing of the pelvis.

The three basic drawings are utilized to establish the locations of left and right points A and B. The vaginal fornices and the longitudinal uterine axis are used to locate point A. The mid-sagittal plane and the fornices are

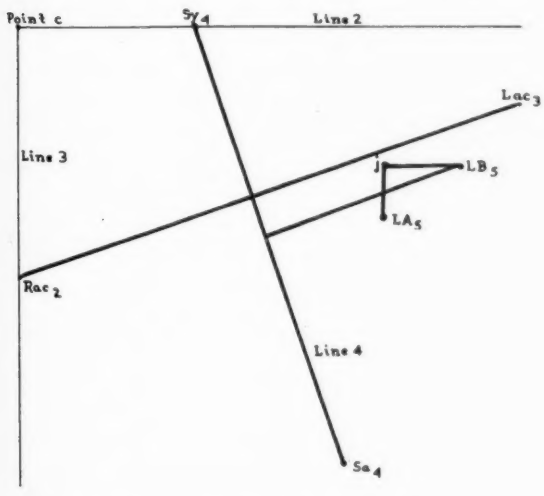

Fig. 15. Transverse plane drawing of the pelvis.

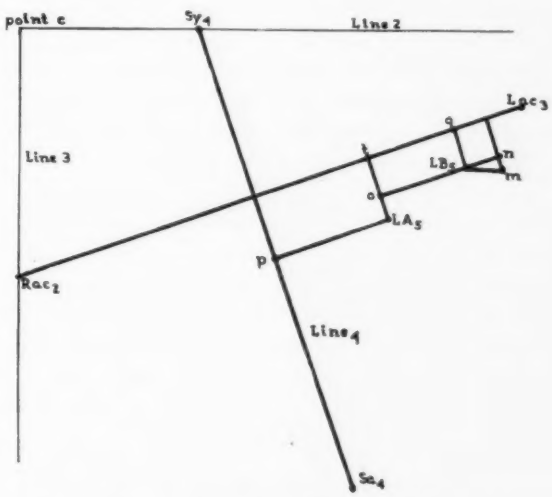

Fig. 17. Transverse plane drawing of the pelvis.

used for point B localization. The images of the radium containers are outlined on the anteroposterior and lateral drawings.

Several steps are required to locate the projection of left point A (LA_1, Fig. 11) on the lateral drawing. The amount of pelvic rotation about the longitudinal axis of the body is determined by the use of the transverse drawing (Fig. 10). Line 5 is drawn perpendicular to line 3 at point Rac_2 (Fig. 10). Line 5 is parallel to the anteroposterior drawing. The angle θ between line 5 and the interacetabular line represents the degree of pelvic rotation with respect to the anteroposterior drawing. Inset 1 of Figure 11 demonstrates the use of the angle of pelvic rotation θ to determine the displacement of LA_1 on the lateral drawing anterior or posterior to the longitudinal axis of the uterus. Point e represents the point of the uterine longitudinal axis where a perpendicular line from point A intersects the axis. Line r_1 is constructed parallel to the anteroposterior drawing. Point A is placed 2 cm. from point e on a line which is at an angle θ with r_1. The length of d represents the displacement of point A anterior or posterior to point e on the lateral drawing.

The images of the vaginal radium capsules on the lateral drawing are used to establish the location of the ovoid images within the vaginal fornices when the plastic ovoids themselves cannot be visualized. When the Ernst applicator is used the most superior vaginal container is utilized to identify the fornix. In every case the anteroposterior roentgenogram is examined to make certain that there is close contact between the images of the vaginal containers and the fornices. A radiopaque clip on the cervix acts as a further check point on the approximation of tissues and containers. The longitudinal axis of the intrauterine radium is utilized to establish the position of the longitudinal uterine axis.

Figure 11 shows the images of the radium containers on the lateral drawing. Point LA_1 is located as the center of a circle, 2 cm. radius, tangent to the images of the ovoids or Ernst applicator. The center of the circle is located distance d (Inset 1) anterior or posterior to the uterine axis depending upon the direction of pelvic rotation. Inset 11 shows a detailed sketch of the region of the circle about point LA_1 and the ovoid image. Length r_2 is a radius (2 cm.) at the point of tangency. Line r_3 is parallel to the anteroposterior drawing and its length is determined by a perpendicular line from it to the point of tangency. The projection of left point A (LA_1) is now fixed on the lateral drawing.

Next, the images of the radium containers are placed on the anteroposterior drawing (Fig. 12). On this drawing point LA_2 is located distance r_1 (Fig. 11, Inset 1) from the longitudinal uterine axis image and distance r_3 (Fig. 11, Inset 11) from the vaginal ovoid image. Distance r_1 is taken perpendicular to the line of the uterine axis image. The direction of r_3 is the same as the direction of the uterine axis image. LA_2 (Fig. 12) represents the projection of left point A on the anteroposterior drawing.* In cases of lateral flexion of the uterus, the superior-inferior relationship of point LA_1 (Fig. 11) requires relocation. The radius of the circle used to establish LA_1 location is shortened as indicated by examination of the anteroposterior drawing of LA_2 and its distance superior to the nearest point of the ovoid image.

To find the projection of left point A on the transverse drawing, in Figure 12 line LA_2-LA_3 is drawn perpendicular to line Rac-Lac. The lateral drawing is returned to, as shown in Figure 13, to establish LA_4 by drawing a perpendicular to line 1 from LA_1. LA_5, the projection of left point A, is established on the transverse drawing (Fig. 10) by measuring distance Sy_3-La_4 (Fig. 13) vertically and distance Rac-LA_3 (Fig. 12) horizontally from point c of Figure 10.

It is now necessary to establish the projection of left point B on the drawings of the three planes. A line 5 cm. long is drawn perpendicular to line 4 so as to pass through LA_5. The termination of this line is called LB_1. A horizontal line is drawn from LB_1 so as to intersect a vertical line from LA_5 at point f. In Figure 14, the anteroposterior drawing is used to draw line 6 parallel to the line Rac-Lac at a distance equal to the length of r_3 (Fig. 11, Inset 11) from the most superior point in the ovoid image. Line 6 intersects the line LA_2-LA_3 or its extension. Starting at this intersection the distance LB_1-f

* The use of distance d and length r_1 as well as the use of the right angle between r_1 and the uterine axis was found to be accurate for all cases with less than 10 degrees rotation of the pelvis about the longitudinal axis of the body. There were 26 cases with more than 10 degrees of pelvic rotation and both anteflexion (or retroflexion) and lateral flexion of the uterus. A more detailed procedure for the location of point A images was utilized in the case with the greatest rotation to check the accuracy of the use of the standard procedure detailed herewith. It was found that the use of the distances r_1 and d, and the right angles between r_1 and uterus as determined by the standard procedure introduced no appreciable error in the 26 cases.

(Fig. 10) is measured laterally to establish on line 6 the point LB_2.

LB_2 is utilized as the first approximation of the projection of left point B on the anteroposterior drawing. The distance of LB_2 from the long longitudinal uterine axis image at point h is measured along line 6 and designated as distance g. In Figure 14, Inset 1, the distance g is used together with the degree of pelvic rotation as found on Figure 10, to determine the anterior or posterior relationship of left point B to the point h on the uterine axis directly medial to point B along the line 6. On Inset 1 in Figure 14, a line (7) intersects line 8 at point h with an angle equal to the pelvic rotation. Line 8 is parallel to the anteroposterior drawing. Distance i is established along a perpendicular line to line 8 at distance g from point h. The anterior or posterior relationship of point B is established by the intersection of line length i with line 7. Point h is located on the lateral drawing (Fig. 13) at the level within the pelvis as noted on the anteroposterior drawing (Fig. 14). A line is drawn on Inset 11, Figure 14, perpendicular to the lateral drawing starting at point h. A second line is drawn parallel to the lateral drawing starting at point LB_2 to intersect the first line at point α. LB_3 (Fig. 13) is established distance LB_2-α superior and a distance i anterior to point h. LB_3 is the projection of left point B on the lateral drawing.

In Figure 13, LB_3-LB_4 is drawn perpendicular to line 1. In Figure 15, LB_5 is at the vertically established distance Sy_3-LB_4 (Fig. 13) from point c and 5 cm. from line 4 along a perpendicular to line 4. LB_5 is the projection of left point B on the transverse plane. A horizontal line from LB_5 and a vertical line from LA_5 are drawn which intersect at point j. On the anteroposterior drawing in Figure 16, LB_6 which represents the projection of left point B on the anteroposterior drawing is located distance LB_5-j along line 6 from the line LA_2-La_3. Line LB_6-LB_7 is drawn perpendicular to Rac-Lac.

To establish the distance of point B from the lateral pelvic wall, the intersection of line 6 with the medial image of the lateral bony wall is noted as point k. In Figure 17 a line is drawn from LB_5 parallel to line 2. The distance LB_6-k (Fig. 16) is measured along this line to establish point m. The direction of this measurement corresponds to the point k relationship with point LB_6 (Fig. 16). Starting at point m a perpendicular line is drawn to the interacetabular line. Starting from LB_5 a line is drawn parallel to the interacetabular line until it intersects the line from point m at point n. The distance LB_5-n represents the minimum lateral distance from point B to the pelvic wall.

The two final drawings provide us with the study data for left point A and left point B relationships to the bony pelvis. In Figure 16, LA_2-LA_3 and LB_6-LB_7 are the superior-inferior distances from left point A and left point B, respectively, to the transverse plane containing the interacetabular line. In Figure 17, lines are drawn from LA_5 and LB_5 perpendicular to the interacetabular line to establish points t and q. Lines parallel to the interacetabular line from LA_5 and LB_5 establish points p and o. This figure provides the following measurements: anteroposterior distances of left point A and left point B from the coronal plane containing the interacetabular line as given by lines LA_5-t and LB_5-q, respectively; the distance of left point A from the mid-sagittal plane as given by the line LA_5-p; the lateral displacement of left point B from left point A as given by the length of line LB_5-o; the distance of left point B from the lateral pelvic wall (minimum value) as LB_5-n.

In order to establish the location of right points A and B the same procedures are followed as detailed for the left side. The image locations for point A, LA_2 in the anteroposterior drawing and LA_1 in the lateral drawing are utilized together with the images of the ureters, which are added to the same drawings to determine the spatial relationships for left and right point A and the ureter. After locating both left and right points A and B within the pelvis, actual exposure dose rates at these points are determined by establishing the distances from each radium capsule in the applicator to the points and referring to standard linear radium dose rate tables for r/mg.hr. values.

George C. Lewis, Jr., M.D.
Hospital of the University
of Pennsylvania
3400 Spruce Street
Philadelphia 4, Pennsylvania

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ISODOSE CURVES FOR CERTAIN RADIUM APPLICATORS USED IN THE TREATMENT OF UTERINE CERVICAL CANCER*

By NORMAN A. BAILY, PH.D.,† *and* VIRGIL E. YODER, M.S.
BUFFALO, NEW YORK

ALTHOUGH radium has been in use for the treatment of gynecologic cancer for many years, experimental dosage determinations are scarce. In roentgen therapy experimentally determined isodose curves are universally used. For most radium applicators these do not exist. Some reasons for this are: first, the difficulty in making such curves and, secondly, the great variety of physical sizes and types of applicators with their varied loadings which are in use in the different treatment centers.

This deficiency was recognized early by Lucas[4] who attempted to calculate such dose distributions in terms of skin erythema units. It was again pointed out by Mayneord and Honeyburne[5] who developed a rather complex method to calculate these more accurately. In 1944, Quimby[8] published her now famous tables for linear sources. These facilitated the computation of complex arrangements. One of the first attempts at experimental determinations was made for certain applicators by Nolan and Natoli.[7] These authors introduced a system of photographic film dosimetry. Using an ionization chamber in conjunction with a water phantom, Walstam[10] determined isodose curves for a number of radium arrangements then in use at the Radiumhemmet. A comprehensive study of various combinations of radium sources loaded in an expanding type cervical uterine applicator has recently been published by Ernst.[1]

APPLICATORS STUDIED

The isodose curves to be presented in this paper represent two basic applicators which are commonly used in this Institute and also are found in many treatment centers throughout this country. Isodose curves for various loadings of these applicators have been determined. The two applicators are shown in Figure 1, *A* and *B*. These applicators have a straight tandem portion capable of holding either one, two, or three cells. The applicator shown in Figure 1*A* has a perpendicular cross arm at one end of the tandem capable of holding a single cell. The cell in the cross arm is positioned on the axis of the tandem with its axis located 2 mm. above the end of the last cell in the tandem. The applicator shown in Figure 1*B* is made to take two cells at the end of the tandem with their axes parallel to each other and separated by 1.2 cm. Both applicators are made of stainless steel having a wall thickness of 1 mm. The cells used in this study contained 15 mg. of radium filtered by 1 mm. platinum, with an active length of 1.5 cm. and a total length of 1.7 cm. The diameter of the cells is 4 mm.

METHOD

The isodose curves to be presented here were obtained using photographic film.[2,3,9,11] The use of photographic film in a masonite phantom offers several advantages over the use of an ionization chamber or scintillation probe in conjunction with a water phantom. First, exposure to the investigator can be reduced considerably. Secondly, the time necessary to obtain curves with the same degree of accuracy is substantially reduced. Thirdly, the position of the applicator with respect to the film is easily and accurately determined.

While it is well known that the response of photographic film is strongly wavelength

* From the Department of Radiation Therapy, Roswell Park Memorial Institute, Buffalo, New York.
† Present Address: Nuclear Electronics Laboratory, Hughes Aircraft Company, Culver City, California.

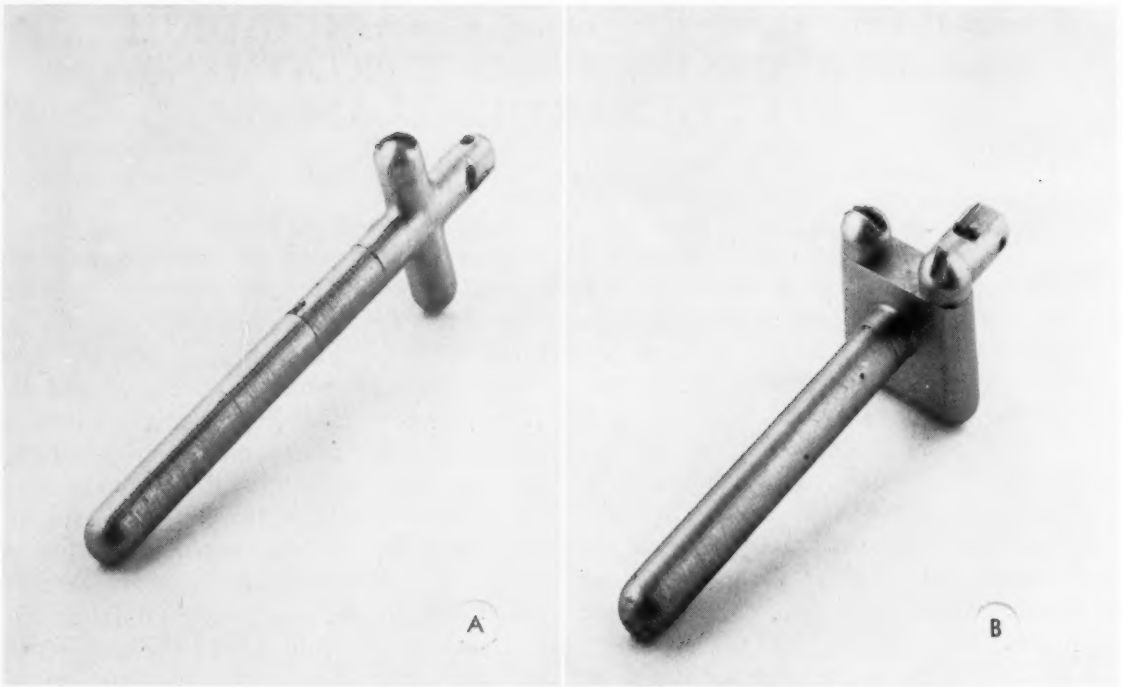


Fig. 1. Radium applicators for use in the treatment of cancer of the uterine cervix. (*A*) Tandem with single cross bar. (*B*) Tandem with double cross bar. The double cross bar accommodates two radium cells separated by 1.2 cm. between centers.

dependent in the region below an energy of about 0.3 mev., this dependence does not pose a serious problem when used with the gamma rays of radium.[2] However, due to scattering and degradation of the radiation within the phantom, this is only true at distances where the exposure is mainly due to the primary radiation. At greater distances from a radium source placed in such a phantom, a large proportion of the exposure may be due to scattered radiation. Because of the longer wavelengths present in this radiation and the enhanced response of the film for these energies of radiation, dosage measurements can be in error.[9] It has been shown that for the materials and techniques used in this investigation and for distances up to 10 cm. from the source, measurements made with film were in good agreement with those made with an ionization chamber in a water phantom.[11] As a further precaution against errors arising from this source, all calibration films were exposed in the masonite phantom. Therefore, films exposed both for calibration purposes and those exposed using the applicators under investigation should have received primary and scattered radiation in the same proportion.

The photographic film used was du Pont "Adlux." This film was chosen because its slow speed allows conveniently long exposure periods and because its response characteristics had been fully investigated.[11] When film density is plotted against the logarithm of the exposure, a typical Hurter-Driffield curve is obtained.[6] The linear portion of this curve extends approximately from 80 to 800 r. The exposure time used was four hours, since it had been determined that this period of exposure would give densities falling on this linear portion for distances from the source which are of clinical interest. This was true with but one exception where a dose rate of 10 r per hour was encountered. The films were developed in Kodak liquid x-ray developer for five minutes at 20° C., using intermittent agitation.

Three phantoms were used so that films

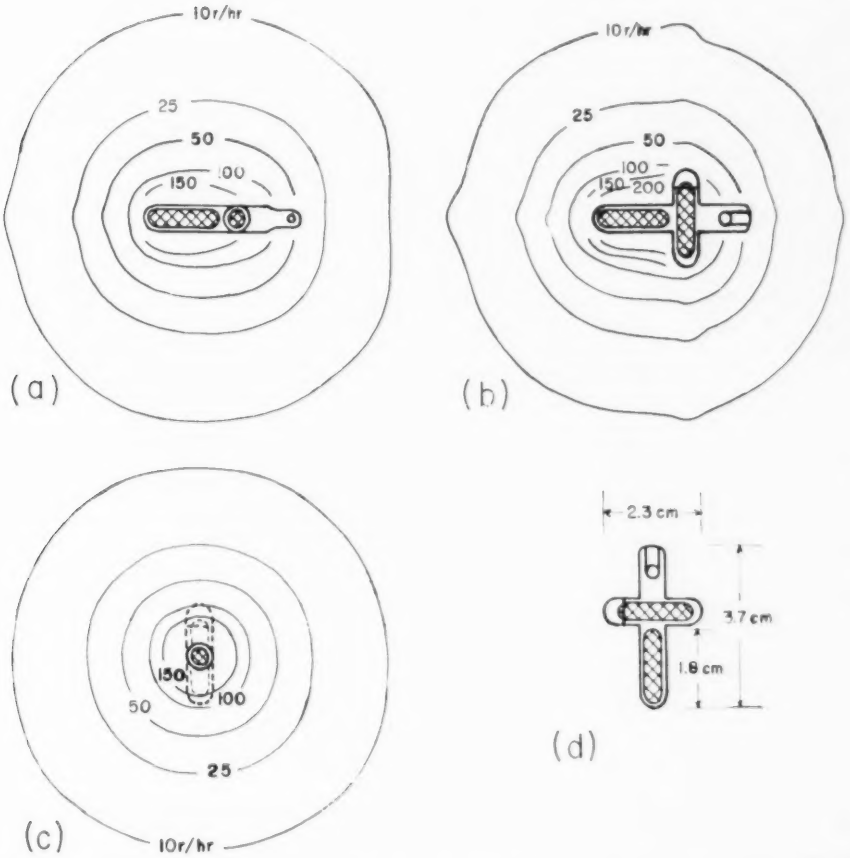
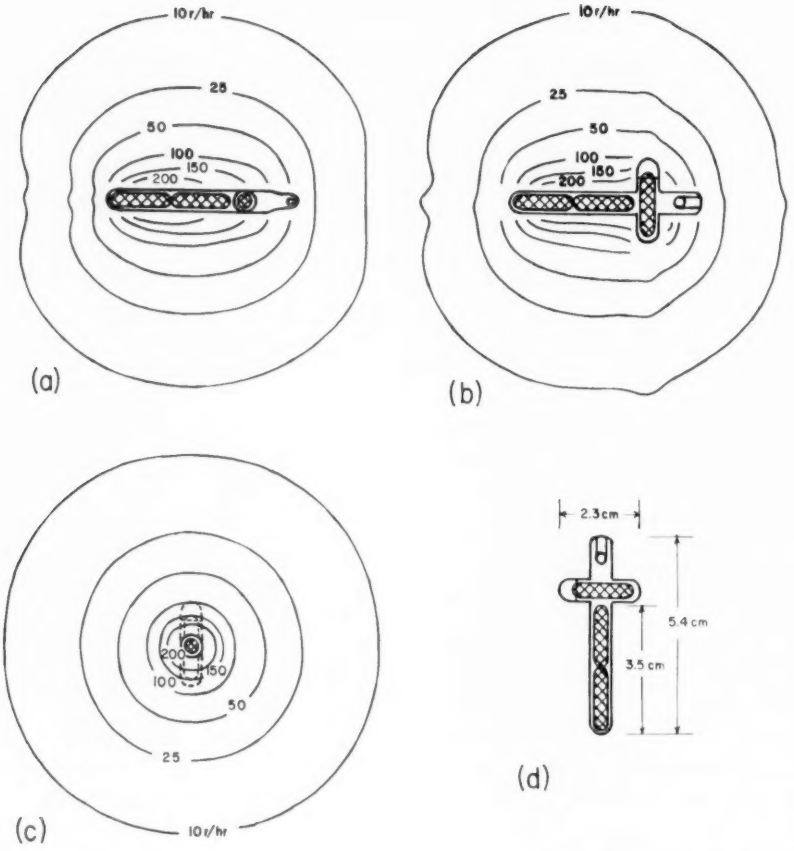


Fig. 2. Tandem with single cross bar (*A*). Isodose curves for a tandem applicator composed of a single 15 mg. cell having a cross arm containing one 15 mg. cell. (*a*) Isodose curves in a plane passing through the axis of the tandem and perpendicular to the cross arm. (*b*) Isodose curves in the plane passing through the axis of the tandem and parallel to the cross arm. (*c*) Isodose curves in the plane perpendicular to the tandem and passing through its midpoint. (*d*) Cross-section of applicator. All dose rates are given in r per hour.

in both planes and a calibration film codly be exposed and developed simultaneousul and then read in succession. These phantoms were constructed using 5/32 inch sheets of tempered masonite having a density of 0.988 gm. per cc. Their dimensions were 28 cm.×36 cm.×12 cm. The phantoms were cut out to the exact dimensions of the calibration cell and the applicators, respectively. The calibration cell was held with its axis perpendicular to the film while each of the two phantoms held the applicator axis perpendicular or in the plane of the film. In the case of the applicators, the portion of the phantom holding the applicators was enlarged to accommodate the size applicator being studied as the investigation proceeded.

The calibration film was used so that any changes in film processing from experiment to experiment would not cause error. The films used for this purpose were always taken from the same box as those being used with the applicators. The calibration source contained 25 mg. of radium distributed over a length of 9 mm. and was filtered by 1 mm. of platinum.

The densities on the calibration film were related to the actual dose in roentgens through the use of the Quimby[8] tables and a correction factor for degradation and scatter within the phantom. This correction factor was determined by taking ionization chamber readings in air and also


10r/hr
25
50
100
150
200
(a)
10r/hr
25
50
100
150
200
(b)
200
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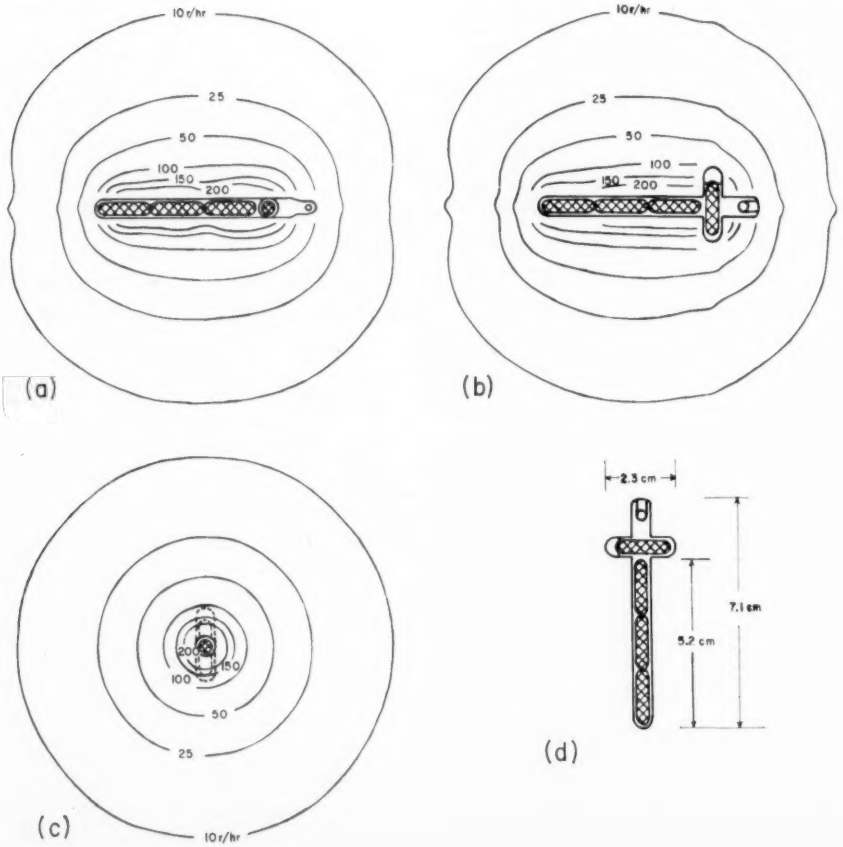
25
10r/hr
(c)
2.3cm
5.4cm
3.5cm
(d)


10r/hr
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(a)
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(b)
200
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100
50
25
10r/hr
(c)
2.3cm
7.1cm
5.2cm
(d)

FIG. 3. Tandem with single cross bar (*A*). Isodose curves for a tandem containing two 15 mg. cells and a cross arm containing one 15 mg. cell. (*a*) Isodose curves in the plane which passes through the axis of the applicator perpendicular to the cross arm. (*b*) Isodose curves in the plane passing through the axis of the applicator parallel to the cross arm. (*c*) Isodose curves in the plane perpendicular to the axis of the tandem and passing through its midpoint. (*d*) Cross-section of applicator. All dose rates are in r per hour.

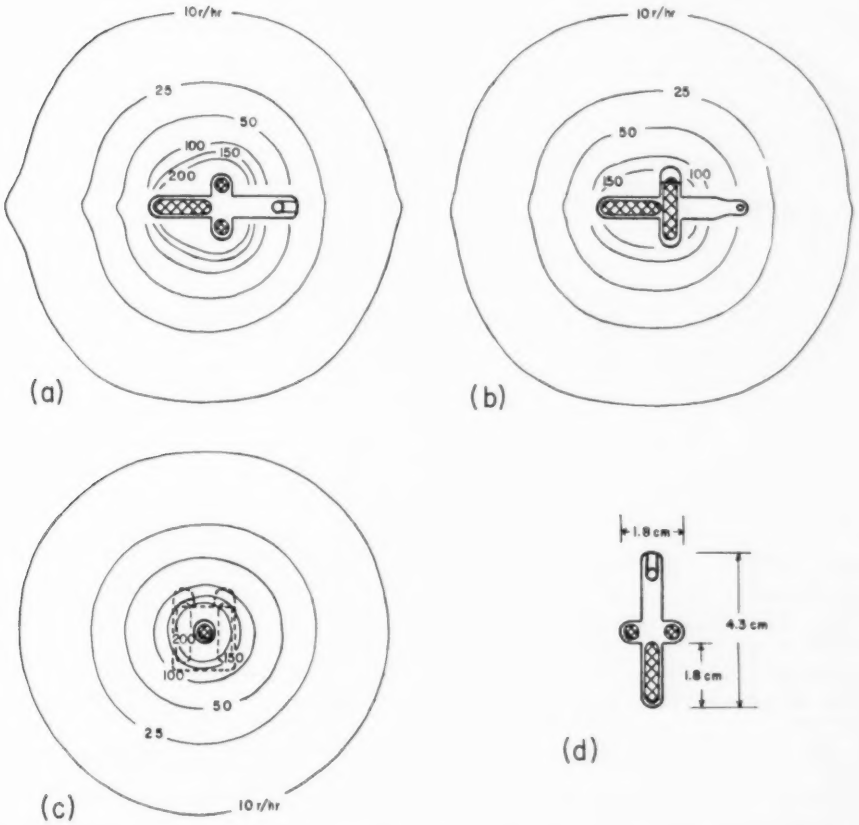

FIG. 5. Tandem with double cross bar (*B*). Isodose curves for a tandem applicator composed of one 15 mg. cell and two 15 mg. cells placed in a cervical face plate. (*a*) Isodose curves in a plane passing through the axis of the tandem and perpendicular to the axis of the cells in the face plate. (*b*) Isodose curves in a plane passing through the axis of the tandem and parallel to the axis of the two cells in the face plate. (*c*) Isodose curves in a plane passing through the midpoint of the tandem and lying perpendicular to the axis of the tandem. (*d*) Cross-section of applicator. All dose rates are given in r per hour.

FIG. 4. Tandem with single cross bar (*A*). Isodose curves for a tandem applicator containing three 15 mg. cells in tandem and one 15 mg. cell in the cross arm. (*a*) Isodose curves in the plane passing through the axis of the tandem and perpendicular to the cross arm. (*b*) Isodose curves in the plane passing through the axis of the tandem and parallel to the axis of the cross arm. (*c*) Isodose curves in the plane perpendicular to the axis of the tandem and passing through its midpoint. (*d*) Cross-section of applicator. All dose rates are in r per hour.

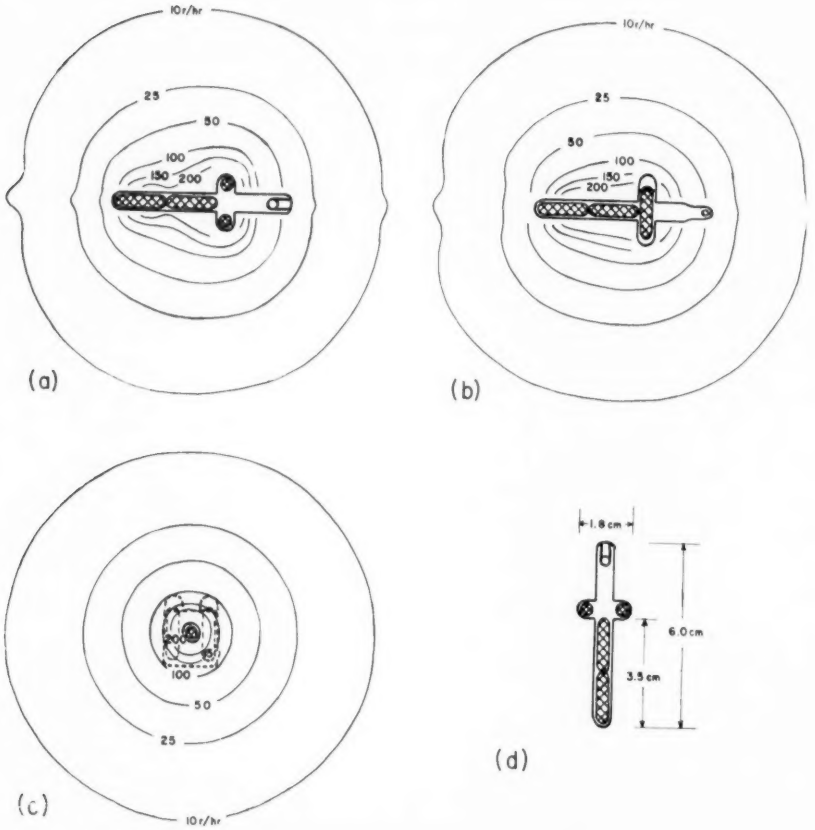

FIG. 6. Tandem with double cross bar (*B*). Isodose curves for a tandem applicator containing two 15 mg. cells in tandem and two 15 mg. cells in a cervical face plate. (*a*) Isodose curves in a plane passing through the axis of the tandem and perpendicular to the axis of the cells in the face plate. (*b*) Isodose curves in a plane passing through the axis of the tandem and parallel to the axis of the cells in the face plate. (*c*) Isodose curves in a plane passing through the midpoint of the tandem and lying perpendicular to the axis of the tandem. (*d*) Cross-section of applicator. All dose rates are given in r per hour.

within the phantom at distances ranging between 2 and 10 cm. from the source. The ratio of phantom to air values was determined to be 0.95 ± 0.01.

Film densities were measured using an Ansco-Sweet densitometer with a 3 mm. aperture. Although density differences could be detected for film movements as small as 0.5 mm., it must be pointed out that all values determined are really averages over the area covered by the aperture. Using the calibration film which had been exposed to the standard 25 mg. source, a density versus total dose curve was established. The densities of the experimental films were then read and transcribed in terms of the roentgen dose using the above curve. Isodensity points previously marked out on the film and connected by smooth curves were then traced to produce the isodose curves.

RESULTS

The isodose curves obtained by the method described above are shown in Figures 2 through 7. In each of these figures the isodose curves shown under (*a*) represent the dose rates in roentgens per hour in a plane passing through the axis of the tandem and perpendicular to the cells placed at the end of the tandem. Those shown under (*b*) are those obtained at 90° to those in (*a*). The isodose curves shown under (*c*) would be those that are found in

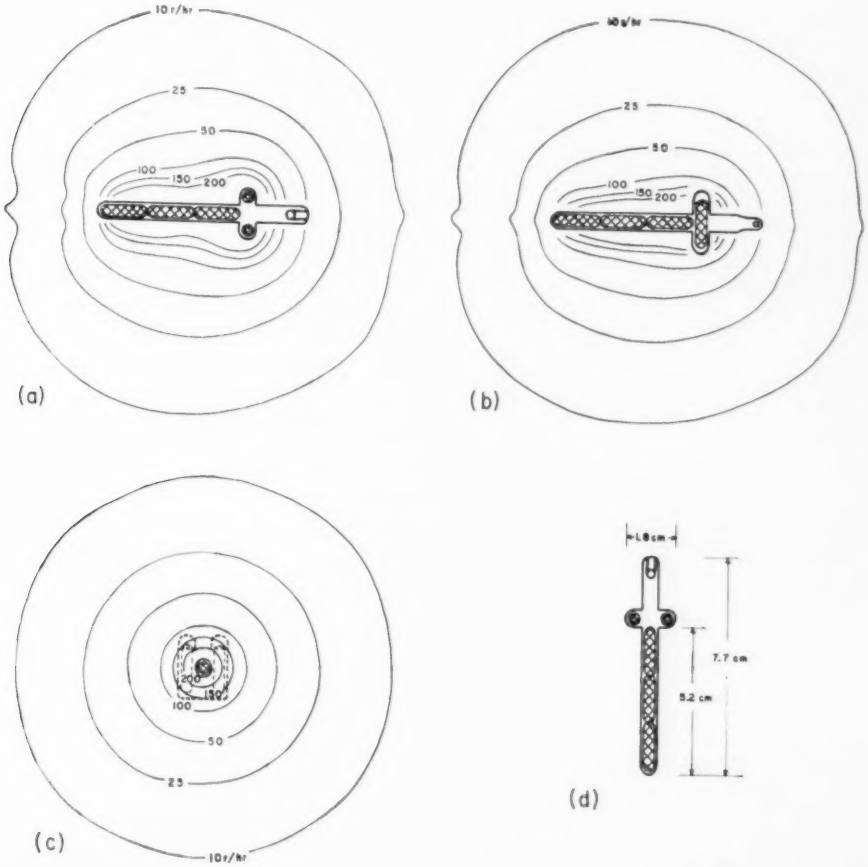

Fig. 7. Tandem with double cross bar (*B*). Isodose curves for a tandem applicator containing three 15 mg. cells in tandem and two 15 mg. cells in a cervical face plate. (*a*) Isodose curves in a plane passing through the axis of the tandem and perpendicular to the axis of the cells in the face plate. (*b*) Isodose curves in a plane passing through the axis of the tandem and parallel to the axis of the cells in the face plate. (*c*) Isodose curves in a plane passing through the midpoint of the tandem and lying perpendicular to the axis of the tandem. (*d*) Cross-section of applicator. All dose rates are given in r per hour.

a plane lying perpendicular to the axis of the tandem and passing through the midpoint of the tandem. (*d*) in each case is a cross-sectional view of the applicator showing the location of the active cells.

SUMMARY

Isodose curves are presented for uterine cervical radium applicators having various length tandems. For each size tandem studied, curves are presented for three different planes; (*a*) the plane passing through the axis of the tandem and lying perpendicular to the cross cells, (*b*) the plane passing through the axis of the tandem and lying parallel to the cross cells, and (*c*) the plane passing through the midpoint of the tandem and lying perpendicular to its axis.

Norman A. Baily, Ph.D.
Nuclear Electronics Laboratory
Hughes Aircraft Company
Culver City, California

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TEFLON TUBE METHOD OF RADIUM IMPLANTATION*

By OSCAR L. MORPHIS, M.D.†
FORT WORTH, TEXAS

THE radiation hazard to the physician using radioactive isotopes, and particularly radium, has become an increasing problem. Many physicians have found that the amount of radiation received during an interstitial implantation of low intensity radium needles was close to the weekly tolerance of 300 mr, thus limiting the number of cases that could be performed.

Since "necessity is the mother of invention," a method of interstitial implantation of radium has been worked out giving the operator a maximum opportunity for laying out the ideal radiation pattern and limiting the exposure of the operator and the operating room personnel to a minimum amount of radiation. Briefly, the method consists of sewing Teflon tubing through the tissues and completely laying out the desired radium pattern. After this pattern is complete and all tubes are in place, one end of the tube is sealed with a Michel clip. The tubes are filled with the radium or other radioactive material and then the other end is sealed with a Michel clip. The exposure of operating room personnel to radioactivity is usually less than five minutes.

The first problem encountered was in designing a needle to hold the Teflon tubing securely. A Steinmann pin, $\frac{7}{64}$ inch in diameter, proved to be the correct size. The end of the pin is turned down in a lathe to .088 inch. A No. 2-56 die, opened to full capacity by regulating the adjustment screw on the die, is used to cut a thread on the shaft, thus converting the Steinmann pin to a sewing needle (Fig. 3). Polypenco spaghetti tubing No. 13 (Teflon) which has an internal diameter of .076 ± .003 inch and a wall thickness of .14 ± .003 inch, is

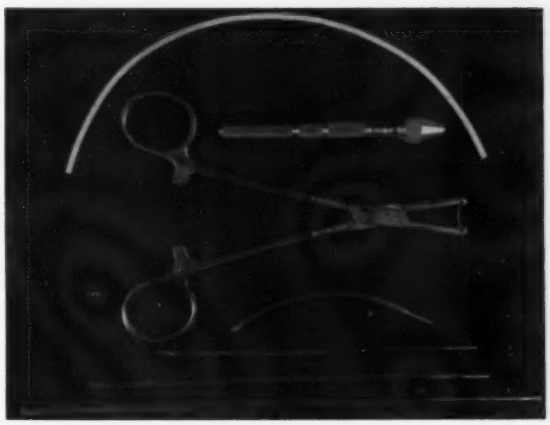

FIG. 1. Needles, Teflon tubing, Lufkin pin vise, forceps and Michel clips used for implantation of radioactive materials.

FIG. 2. *Upper:* Machined end of Steinmann pin and Teflon tube ready to be joined together. *Lower:* Steinmann pin and tube joined so as to form an atraumatic suture.

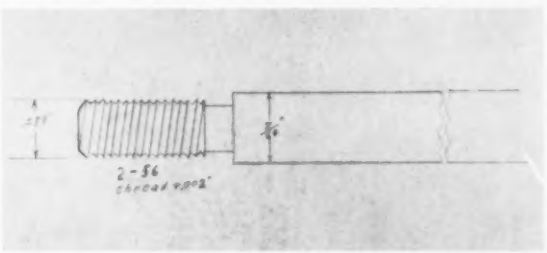

FIG. 3. Detailed drawing of machined and threaded end of Steinmann pin.

* Presented at the Fortieth Annual Meeting of the American Radium Society, Hollywood, Florida, March 27–29, 1958.

† Member, Tom B. Bond Radiological Group, Associate Clinical Professor of Radiology, University of Texas, Southwestern Medical School.

Fig. 4. Needle and Teflon tube held in pin vise.

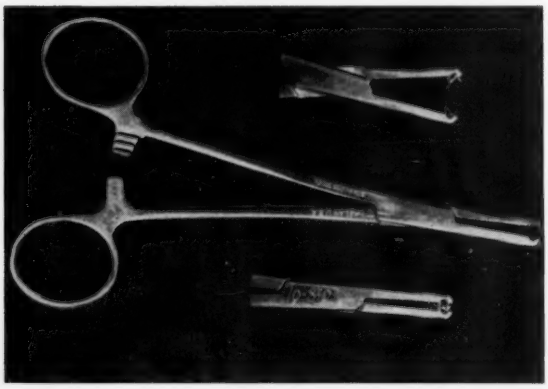

Fig. 5. Forceps with No. 36 wire gauge hole in jaw to hold Teflon tubing without crushing its wall and to fasten Michel clips to ends of tubes.

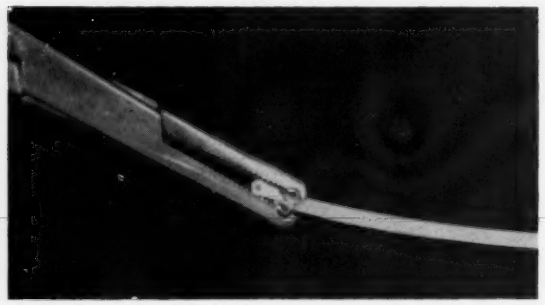

Fig. 6. Forceps sealing end of Teflon tubing with Michel clip.

almost exactly $\frac{7}{64}$ inch in outside diameter so that the outside diameter of the needle and the outside of the tubing match, and the needle and tubing will slip through the tissue in an atraumatic fashion.

Many other materials were tried, but Teflon was the only one fulfilling the requirements. The characteristics of Teflon that made it desirable for this procedure are: (1) stability to withstand heat up to 550° F., thus allowing all materials to be autoclaved; (2) resistance to stretching so that its diameters are not easily altered; (3) a tube wall stiff enough to remain fastened securely to the threaded end of the needle; (4) secondary scatter similar to that of tissue; and (5) smooth and slick walls, allowing the radium needles to be inserted easily.

One can insert accurately the needle through any portion of the body that will lend itself to a through-and-through suture. The needles can be made in any desired length, but a needle from 6 to 9 inches in length has proved most useful. The needles can be curved to any desired shape for passage through irregular areas, such as under the chin. The point of entrance and the

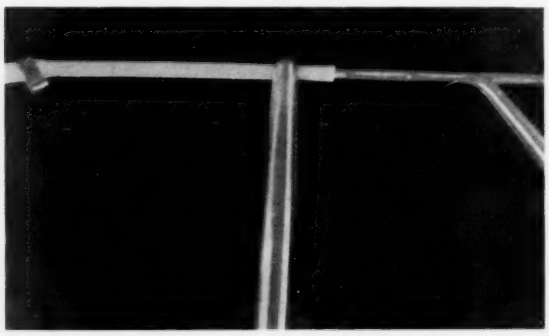

Fig. 7. Low intensity needle inserted into Teflon tubing. The eye of the needle is inserted first.

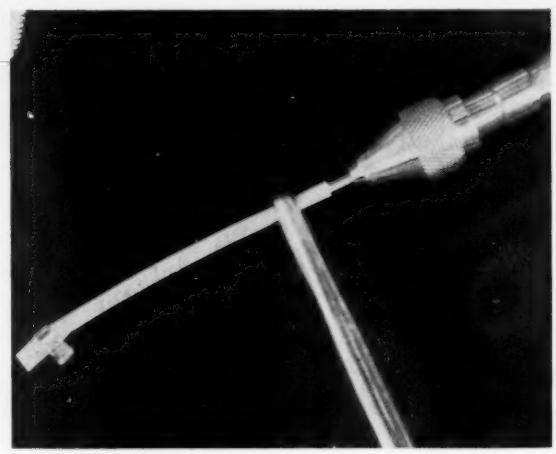

Fig. 8. Stylet pushing the radium needle to its proper position.

point of exit are clearly defined and the path of the needle is easily determined. The path of previously implanted tubes is so well defined that a good geometric pattern is readily obtained without resorting to time-consuming roentgenographic control studies in the operating room.

A Lufkin pin vise (Fig. 4) with a maximum capacity of $\frac{1}{8}$ of an inch has proved most useful as a handle for inserting the needle through the tissue. This vise is slipped over the needle and tightened down on its shaft; the Teflon tubing is screwed on to the threaded end and the pin vise is used to insert the needle (Fig. 10). The Collet chuck of the pin vise is loosened, slipped over the back end of the needle and pulled off the Teflon tubing. The Teflon tubing is then pulled into place and long ends are left protruding through the skin (Fig. 11).

A pair of forceps for handling the tubing has been made by reclaiming a pair of heavy discarded forceps from the operating room and cutting and rounding the jaws (Fig. 1 and 5). A hole is drilled with a No. 36 wire gauge drill, so that half of the hole is in each jaw. This will grasp the tubing without compressing the walls. This clamp is also used to fasten the Michel clip to the ends of the tubing (Fig. 6).

Fig. 10. Special needle held in pin vise is inserted through the lesion. The examining finger determines the course of the needle through the tissue.

Fig. 9. Patient with squamous cell carcinoma of the buccal mucosa being prepared for radium implantation.

Fig. 11. The Teflon tubing is pulled into place and a segment of the tubing of the desired length is left in the tissue with its ends protruding through the skin.

FIG. 12. The entire radium pattern is laid out and one end of the tube sealed with Michel clips.

FIG. 13. Low intensity radium needles are inserted into the open ends of the tubes using the special forceps to hold the end of the tube while inserting the radium needle (eye end first). The needle is pushed into its proper position using a stylet and the open end of the tube is sealed with Michel clips.

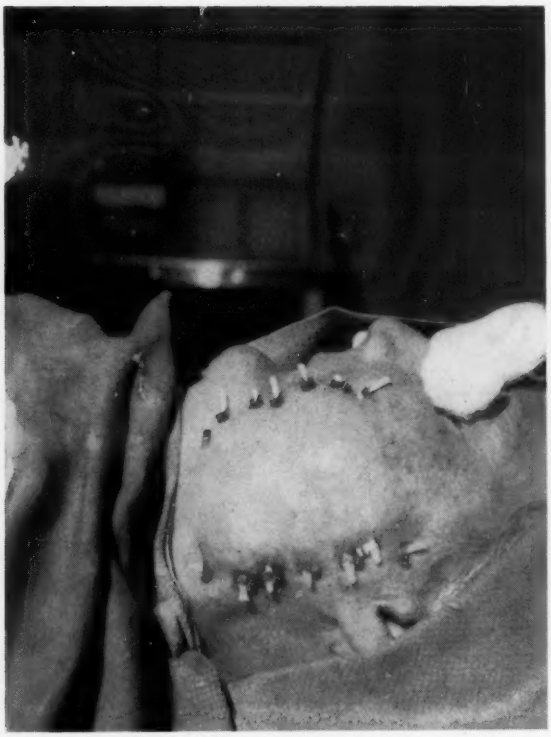

FIG. 14. The operation is complete, the tubes are filled with radium and Michel clips seal the radium inside the tubes and prevent the tubes from changing positions.

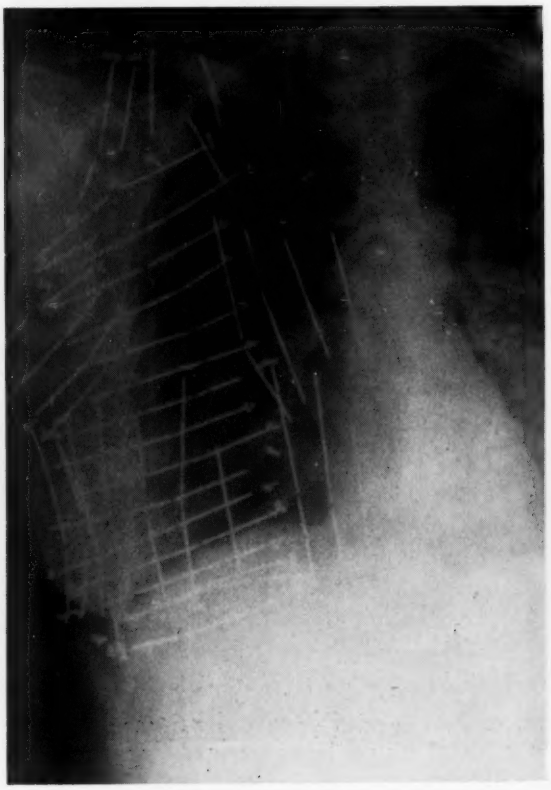

FIG. 15. Extensive inflammatory carcinoma of the breast.

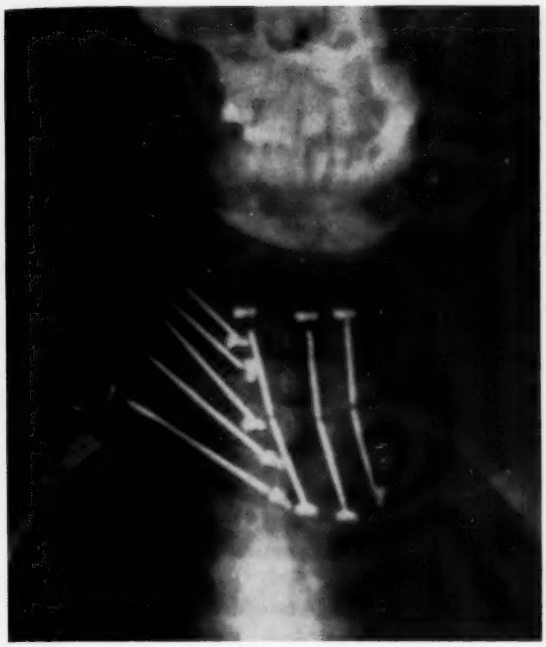

Fig. 16. Carcinoma of the thyroid with a metastatic lymph node.

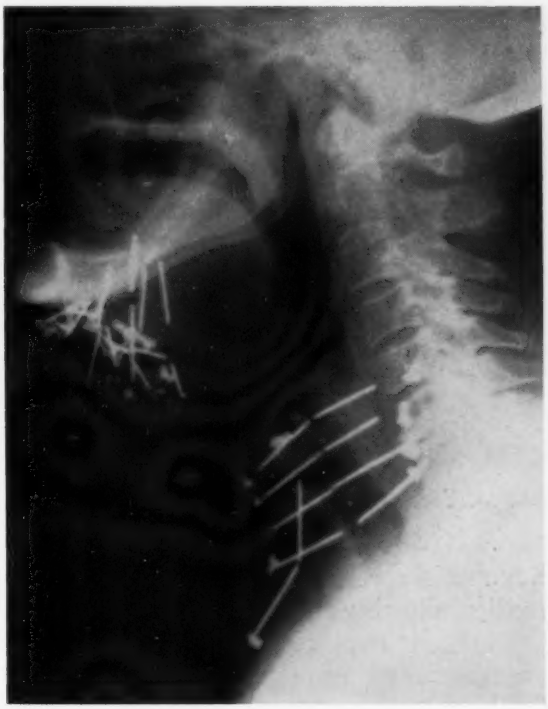

Fig. 17. Lymphosacroma implant after lesions had become completely resistant to roentgen-ray therapy.

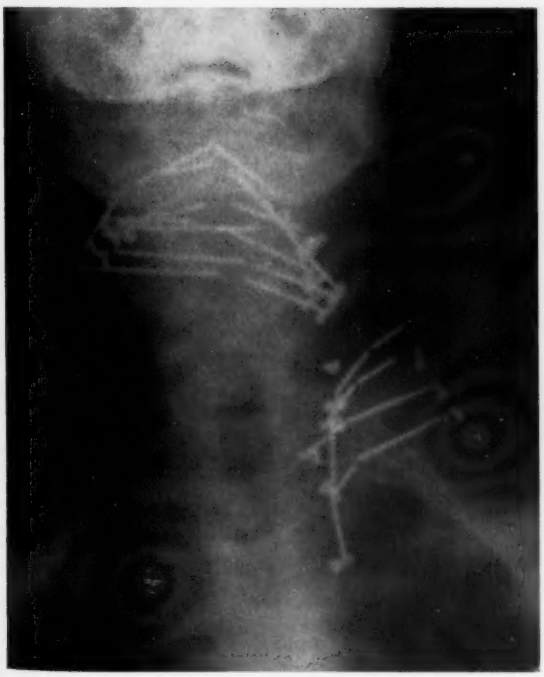

Fig. 18. Same case as in Figure 17 showing the way the Teflon tubes are inserted in a curved fashion through the base of the tongue.

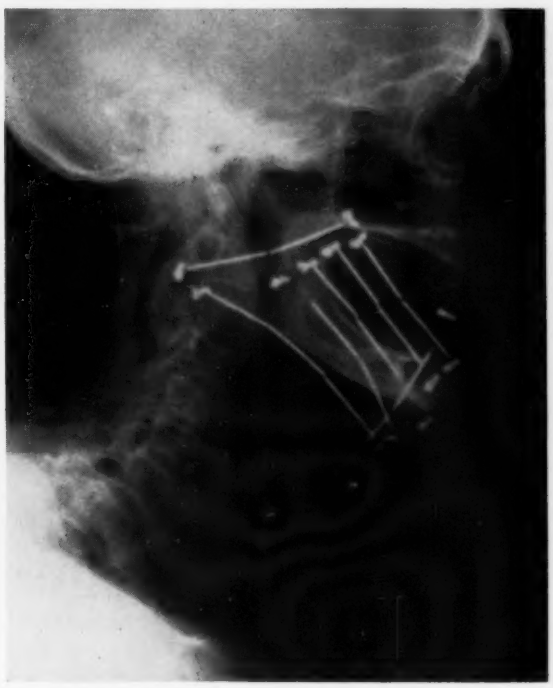

Fig. 19. Carcinoma of the buccal mucosa.

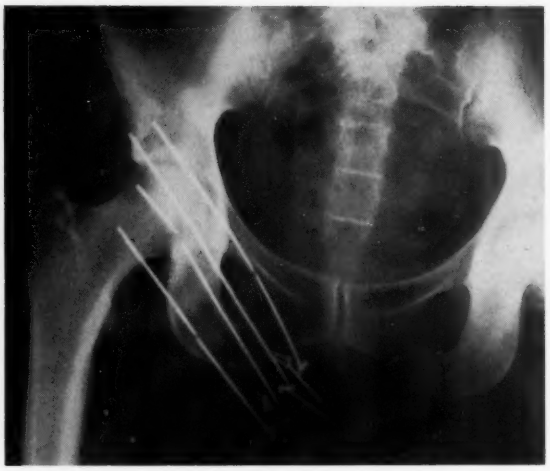

Fig. 20. Carcinoma of the vulva with a metastatic lymph node in the inguinal region.

A special forceps for handling the radium needles, allowing one to pick up the needle and lock it in place with a thumb latch, was furnished by the radium suppliers. The radium is inserted in the Teflon tubing by grasping the tubing with the forceps described above and by placing the needle in the tubing with the eye entering the tubing first (Fig. 7 and 13). If the point of the radium needle is inserted first it may cut through the Teflon tubing wall. The radium-handling forceps is released and the needle inserted to its proper location using a stylet (Fig. 8). The stylet is made of a Steinmann pin of such diameter that it will pass easily through the tubing without binding. The ends of this stylet are slightly counter-bored so as to retain the point of the needle during the process of placing it to its proper location. After the radium is placed in each individual tube, the end of the tubing is sealed with a Michel clip (Fig. 14).

The tubes containing the radium are easily and quickly removed by sterilizing the area with an antiseptic and cutting off one end of the tube—with its Michel clip—with a pair of scissors and slipping the entire tube out of the patient. Technicians receive a minimum of exposure in removing, cleaning and storing the needles.

Over 100 cases of carcinoma of various portions of the body have been treated using this technique since August, 1956.

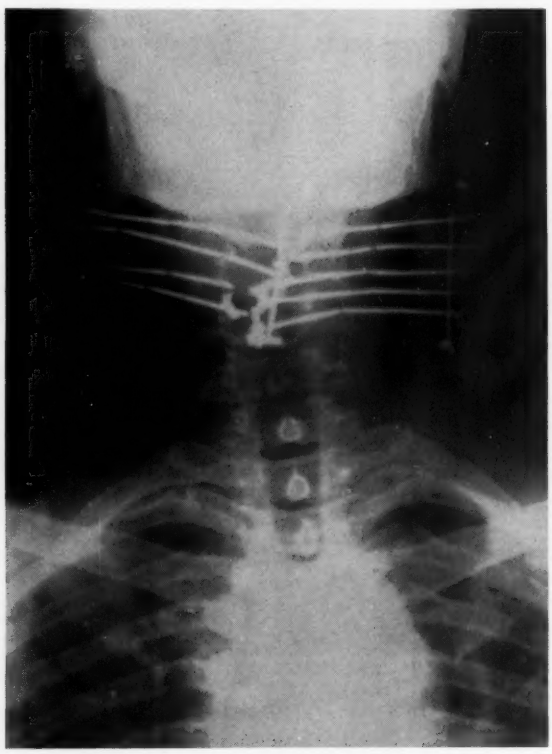

Fig. 21. Metastatic squamous cell carcinoma of lymph nodes, bilaterally.

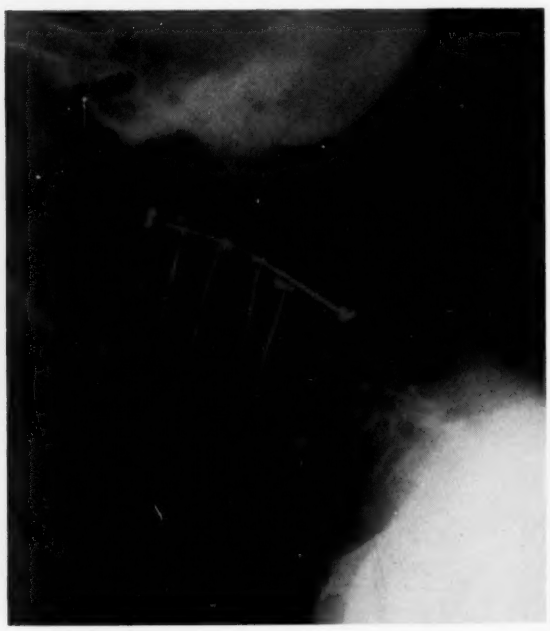

Fig. 22. Metastatic squamous cell carcinoma in the cervical lymph nodes, secondary to carcinoma of the tongue.

Figures 15 through 22 demonstrate radium patterns used in various portions of the body.

SUMMARY

A method of implanting low intensity radium needles in a pre-arranged pattern, employing Teflon tubing, is described and offers the following advantages:

1. Good geometric patterns can be laid out accurately while exposing the operator and operating room personnel to a minimal amount of radiation.

2. The hands do not come into close approximation with the radioactive material at any time.

3. The entire procedure can be carried out very rapidly, and exposure to radioactive substance is only that time required to actually fill the tubes with the radioactive material.

4. Technicians receive only a minimal dose of radiation during the preparation of the needles since there is no threading of the needles required. Exposure to the technician occurs only during the time in which the needles are pushed out of the Teflon tubes and washed before storing.

5. The Teflon tubing with its radium contents is easily and quickly removed from the patient, again decreasing the exposure to personnel.

6. The radium pattern within the tubing can be re-arranged easily.

7. A large area can be implanted.

8. The length of a radium needle is no longer a limiting factor as several needles can be used in one tube.

9. All materials can be sterilized by boiling or autoclaving.

815 Medical Arts Building
Fort Worth, Texas

I wish to give recognition to Mr. D. P. Wood of Convair, Division of General Dynamics, for his technical assistance in developing this technique.

FACILITIES FOR HANDLING AND STORAGE OF MEDICAL RADIATION SOURCES IN A LARGE HOSPITAL UNIT*

By NORMAN A. BAILY, Ph.D.†
BUFFALO, NEW YORK

IN MOST hospitals radioactive sources such as radium (permanently encapsulated) have, by custom, been stored in converted safes. Such storage facilities have had many disadvantages and faults. The units are expensive, bulky and heavy. Protection was mainly obtained by having such units lead lined. The radium itself was usually placed in open lead trays. Applicators and needles have been prepared using an L-block.[1] In a hospital where a great quantity of radium is used, such storage and preparation facilities are not satisfactory. The unit to be discussed here was designed for the storage of 1,255 mg. of radium and for the preparation of 1,000 to 1,500 mg. of radium each month. It was devised to provide maximum flexibility and handling ease, as well as adequate protection to the operator and personnel in surrounding areas.

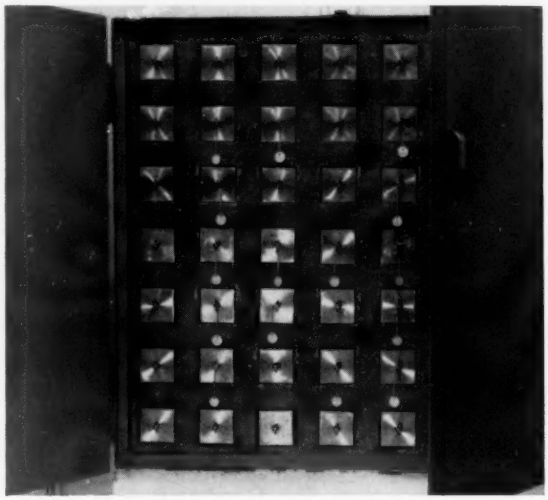

Fig. 1. Radium storage unit.

STORAGE UNIT

The basic storage unit (Fig. 1) was constructed of concrete and has 49 cubicles for the storage of lead containers. The concrete was poured with sufficient thickness for mechanical strength but as thin as possible so that maximum protection would be offered by the lead containers and plugs. In order to prevent powdering of the concrete and to allow easy removal and replacement of the lead pieces, the interior of each cubicle was saturated with shellac. The size of the cubicles is 3×3×8 inches, and the wall thickness of the concrete between the cubicles is 2 inches. The drawers and plugs, which were made of lead-filled stainless steel, and the handling tool are shown in Figure 2. The covers of the drawers provide shielding both during storage and transport. The over-all dimension of the drawer with the cover in place is 3×3×4 inches. Small holes were drilled in the lead (these are not shown in Figure 2) to contain the radium sources, which are cylindrical, ranging in length from 1.0 to 1.5 cm. and having a diameter of 3 mm. The number of sources placed in each unit is dependent on their activity. The drawers have a minimum of 1 inch of lead protection in all directions from the length of the tubes and three quarter inches off the ends of the tube. The amount of radium which can be contained in these drawers ranges from 100 mg. at the center of the unit to 25 mg. at the edges of the unit. The lead plugs which are placed in front of the drawers are necessary in order to keep the dose rate at the front of the unit at a tolerable working level. To keep air spaces to a minimum, the knobs on the drawers, used for attaching the handling rod, were made to nest snugly into the rear of the plug. The plug is also equipped

* From the Department of Radiation Therapy, Roswell Park Memorial Institute, Buffalo, New York.
† Present address: Hughes Nuclear Electronics Laboratory, Culver City, California.

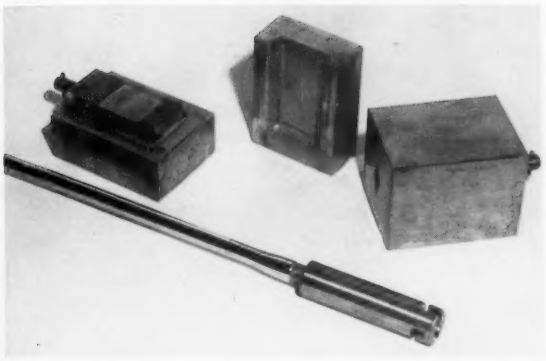

Fig. 2. Radium storage drawer, protective plug, and rod for transport of drawers and removal of plugs from storage unit.

Table I

COMPUTED AND MEASURED VALUES OF THE DOSE RATE AT VARIOUS POINTS ON THE SURFACE OF THE RADIUM STORAGE UNIT SHOWN IN FIGURE 1. A TOTAL OF 1,255 MG. OF RADIUM WAS IN THE UNIT AT THE TIME THE SURVEY WAS MADE

Measured Point (surface)	Measured Dose Rate (mr/hr.)	Computed Dose Rate (mr/hr.)
Center of top	24	—
Center of right side	22	6.4
Center of left side	32	6.4
Center of front face	76	9.6

with a similar knob for use in its removal. The weight of the drawer and plug is 8 pounds. These are comfortably mounted at the end of the handling rod which has a minimum approach distance of 3 feet for the hands.

The number of sources stored in each drawer is governed by their activity. They are placed in the drawer as close to the center as possible, thereby gaining maximum protection from the lead. The sources housed in our unit have activities of 100, 50, 25, 15, 10, and 5 mg. Three drawers, each containing a 100 mg. cell, are placed at the center of the unit. The total activity per container is reduced as the outer surface of the storage unit is approached. The lead plugs shown on the outer perimeter of the unit do not contain radium. These could be placed in use if more storage space were needed by adding concrete to the exterior of the unit. All concrete used in the construction of the unit had a density of 147 pounds per cubic foot.

Before proceeding with the construction of the unit, dose rates at the center of the front surface and at the surface of the side of the unit were computed on the following basis: All sources in each drawer were treated as a point source located at the center of the container. The half-value layers were taken as 1.2 cm. for lead and 6.9 cm. for concrete. These values and also those measured with an ionization chamber calibrated against a radium standard are given in Table 1. The deviation of the measured values from those computed emphasizes the need for a complete survey of every installation before use. This deviation is due to the fact that: (1) all sources in any one container were treated as a point source located at the center of the drawer, and (2) although broad beam half-value layers were used to compute the attenuation through the lead and concrete, no attempt was made to calculate the contribution of additional scatter caused by the large mass of high density material present.

The dose rate at the position of the make-up bench (a distance of approximately 4 feet) is 6.5 mr/hr. The dose rates to the hands, measured with a drawer containing five 15 mg. cells at the end of the handling rod, are 17 and 20 mr/hr. to each hand, respectively.

The make-up shield and apparatus are shown in Figure 3. This apparatus is used in the following way: First, the lead shielding plug and the drawer containing the radium sources are removed from the storage unit and placed on the trolley, which is in position at the rear of the track (Fig. 3). As can be seen, sufficient space has been allowed so that this loading may be accomplished from the side of the shield. The shield has outside dimensions of 24×24×24 inches and is constructed of 2 inch lead. Only the rear and top of the shield are open. The trolley is operated by a remote lever

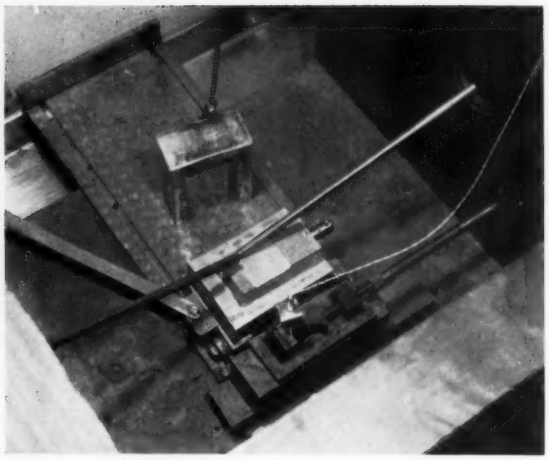

FIG. 3. Shield and apparatus used to prepare applicators containing radium for various clinical uses.

from outside the shield and thus brought into the position shown in Figure 3. To remove the cover, mechanical fingers are used to hook the chain through the ring at the top of the cover. This chain passes through a pulley and is operated from outside the shield. The cover is then raised and set down behind the trolley. The mechanical fingers are also used to guide this manipulation. The chain is then hooked into a support in a taut position so that it does not come loose from the cover. The mechanical fingers enter the shield through clearance holes placed in 2 inch steel balls, which are placed in sleeves and thereby give freedom of motion in all directions. The mechanical fingers are again employed when transferring the radium sources from the drawer to the clinical applicator. The applicator is held in place by a special chuck, which is operated by a rod coming through the shield. The mechanical fingers may be removed and special tools which are employed to assemble the applicators may then be used in the same ball and socket arrangement. The cover is replaced, the trolley moved to the rear and the drawer removed and placed in the storage unit. The loaded applicator is removed using long tongs and placed in the carrier for transport to the operating room.

Measurements which were made with an applicator containing 100 mg. of radium behind the shield were as follows: At the position of the operator's face, 140 mr/hr.; at the level of the thorax, 36 mr/hr.; at the position of the hands, 27 mr/hr.; at the position of the operator's feet, 3.8 mr/hr.

The data indicated below were taken from exposure records, arrived at by film badge monitoring, and were accumulated over the eighteen week period from July 7, 1958 to November 10, 1958. The technician assigned to this work wore two film badges, one on the left thorax and a second on the left wrist. The accumulated dose during this period of time was 770 mr for total body exposure (thorax badge) and 1.59 r for the hands (wrist badge) exposure. These would amount to a weekly average of 43 mr and 88 mr, respectively. On the basis of a forty-eight week year, the doses would be 2.06 r total body and 4.22 r to the hands. These dosage values include all work as described, plus the exposure received during the transfer of radium from the carrier to the storage facility in the operating room, and the exposure obtained in collecting the radium after use and the disassembly of the applicators.

SUMMARY

A unit for storing and incorporating radium cells into clinical applicators and needles has been described. The general approach is also applicable for cobalt 60 sources. The unit embodies economy of construction and can be built on the premises. It provides adequate protection for the work required in a busy hospital radiologic department. A comparison of calculated and measured dose rates is given. Film badge exposure records are discussed.

Nuclear Electronics Laboratory
Hughes Aircraft Company
Culver City, California

REFERENCE

1. National Bureau of Standards, Handbook No. 54. Protection against radiations from radium, cobalt-60, and cesium-137. Supt. of Documents, Washington, D. C., 1954, p. 12.

Vol. 83, No. 3

CHRONIC RADIUM POISONING IN A DIAL PAINTER

CASE REPORT

By JAMES A. GLENN, Jr., M.D.,* JOSEPH GALINDO, M.D.†
GLENS FALLS, NEW YORK
and CLINTON E. LAWRENCE, M.D.
WARRENSBURG, NEW YORK

POISONING due to radioactive substances is constantly assuming greater significance in modern times. Attention has been focused on the ingestion of strontium from fall-out of nuclear weapon testing. Instances have been reported of polonium and plutonium having been absorbed by the human body while being used for industrial purposes. Serious effects have not been demonstrated up to the present but the possibility of irreversible changes exists and should be prevented.

Many dial painters unknowingly loaded their skeletons with lethal amounts of internal radioactive emitters as they worked. These tragedies of the last half century must not be allowed to occur again. Chronic radium poisoning has been exposed, the injurious effects have been emphasized and suitable preventive measures have been instituted.

The case presented in this paper concerns a long term survivor from a group of luminous watch dial painters who were employed in a New Jersey industry more than forty years ago. Radioactive materials were ingested by these painters during the course of their occupation as they pointed their brushes by twirling them between their lips. The formula for the paint was zinc sulfide plus radium and/or mixtures of mesothorium salts. The radioactive compound was added to an emulsion of zinc sulfide and precipitated out with an alkaline sulfate. The radium content was less than 5 mg. per 100 gm. of paint.[7] The painters also were exposed to the radioactive substance by inhalation of the dust of the paint and by absorption through the skin, although probably insignificant amounts were acquired in this manner.

After the paint was swallowed, some of it was absorbed through the small intestines and carried to the viscera, bones, and soft tissues. Radium has a predilection for the skeleton, where it finds permanent lodgement. The bombardment of the bones by the alpha, beta, and gamma rays causes increased brittleness and necrosis.[30] Ewing used the term "radiation osteitis" for the bone destruction and bone production which are characteristic skeletal effects of radium poisoning. Sarcomatous degeneration, carcinomas of the paranasal sinuses, and bone necroses are other ill effects of the body radioactivity. Weakened bone structure inevitably leads to the development of pathologic fractures.

REPORT OF A CASE

B.B., a white female, was born in 1900. In 1917, she was exposed to the absorption of radium salts for fourteen months while employed by a watch dial factory where she painted luminous numerals on the dial faces.

History. After leaving the factory, she apparently enjoyed a healthy life until 1928, ten years from the time of last exposure to radioactive materials. On May 30, 1928, while turning to come up from the basement, her right leg snapped and she sustained a fracture of the middle third of the right femur which required twelve weeks for firm callus formation.

On Thanksgiving Day, 1929, after reaching for a platter on the top shelf of the kitchen cabinet, while stepping down from a stool, she sustained a second pathologic fracture of the right femur, the fracture line being about 3 inches above the previous fracture site. The fracture failed to unite and Dr. Lawrence

* Attending Radiologist, Glens Falls Hospital, Glens Falls, New York.
† Resident Pathologist, Glens Falls Hospital, Glens Falls, New York.

Beisler plated the fracture at The Elizabeth General Hospital, Elizabeth, New Jersey in 1930. The screws did not hold and the plate was removed after five months. In 1930 (for the first time since the original fracture in 1928) it was suspected that her previous occupation as a dial painter was responsible for the bone condition. Dr. Harrison Martland was sought in consultation and he promptly recognized the roentgenographic changes in the right femur as characteristic of radiation osteitis, such as he had seen in many other cases of pathologic fracture in luminous watch dial painters. Dr. Martland referred the case to Dr. Frederick B. Flinn, Director of the Public Health Institute of the College of Physicians and Surgeons in New York City. Measurement of the body burden by the electrometric method showed 15 μg. of radioactive substance. This confirmed Dr. Martland's diagnosis of chronic radium poisoning twelve years after the last exposure to radium dial painting.

In 1931, at the Presbyterian Hospital in New York City, the ununited fracture of the right femur was replated. A bone biopsy at this time showed dense avascular fibrous tissue, very dense bone, and little evidence of necrosis. A roentgen examination at the end of the third week revealed that one of the screws was broken with angulation of the bone fragments. A spica cast was applied. The patient was discharged after six and one-half months with nonunion of the fracture. Pain developed in the left ear before she had left the hospital and necrosis was discovered in the left mastoid. Some drainage was present for several months but this gradually lessened and finally ceased entirely. A skeletal survey showed the chest to be clear. The skull contained multiple moth-eaten areas; the jaw, two areas of bone absorption; the pelvis, scattered areas of bone absorption; the right femur, right tibia, and both shoulder girdles some bone absorption; and the spine, mottling with prolapse of the intervertebral disks into the bodies.

FIG. 1. *Skull:* Roentgenogram taken in 1953, four years before death. There are multiple, irregular, fairly well demarcated areas of bone destruction; normal sella turcica and clinoids; thin occipital and parietal bones; markedly atrophied alveolar processes; absence of all teeth.

In 1931, jaw pain developed and some teeth were extracted. Eventually, all teeth were removed because of partial absorption of the roots.

In 1934, Dr. Darrach removed the vanadium steel plate from the right femur. Five of the six screws had broken. Tissue removed showed radium necrosis of bone.

In 1935, a body burden of 3.9 μg. of radium was measured by Dr. Flinn.

In 1937, roentgenograms showed an incomplete pathologic fracture of the middle third of the left femur. In the same year, a piece of bone was removed from her mandible.

Another measurement of the body burden in 1940 showed 8 μg. of radium.

A fracture of the right clavicle and a rib occurred in 1941.

In 1945, a hysterectomy and appendectomy were performed at the Glens Falls Hospital, Glens Falls, New York, by Dr. LeRoy Butler. Leiomyomata were found.

In 1949, roentgen studies at Dr. Birdsall's office in Glens Falls showed extensive radium necrosis of bone involving the pelvis, extremities, spine, mandible and skull.

A fracture of the left clavicle was treated at home by Dr. Blaney Blodgett of Chestertown, New York, in 1952. This healed spontaneously.

Headache developed in 1953 and she was restudied at the Glens Falls Hospital with skull roentgenograms. Progressive bone destruction was noted by comparison with earlier roent-

genograms, but there was no evidence of intracranial tumor.

The headaches became worse and she was admitted to the National Institutes of Health, Bethesda, Maryland, on February 18, 1954.

Upon admission to the clinical center, the radon excretion in her expired air indicated a body burden of 7.4 μg. of radium. The gamma radiation gave a measurement of 8 μg. She complained of cricket-like sounds in her ears which had persisted since the mastoiditis of 1941, and the headaches which had been retro-orbital since 1953 had shifted to the left temporoparietal region in April, 1954, tending to radiate into the face. There was associated redness of the left eye with tearing and stuffiness of the left nasal passage.

Physical examination revealed the right leg to be shortened and useless. The mouth was edentulous; the thyroid contained a small nodule. A grade 1 systolic murmur was heard at the left sternal border. There was a midline hysterectomy scar. The back showed a marked right dorsolumbar scoliosis.

Laboratory Data. December, 1954: Hemoglobin 10.9 gm. per cent; white blood cell count 5,900; platelets 318,000; bilirubin 0.2 mg. per cent; calcium 9.6 gm. per cent; inorganic phosphorus 3.1 gm. per cent; alkaline phosphatase 2.7 Bodansky units; total protein 6.2 gm. per cent; albumin 3.4 gm. per cent; globulin 2.8 gm. per cent; blood urea nitrogen 10 mg. per cent. Spinal fluid: No white blood cells, total protein 24 mg. per cent, culture negative. Urinalysis: pH 6.0, specific gravity 1.012; albumin negative; sugar negative; occasional epithelial cells; bromsulphalein 3 per cent retention. Cephalin flocculation negative. January, 1955: Phenolsulfonphthalein: 22 per cent of dye excreted in thirty minutes. February, 1955: Serum iron: 48 μg. iron/100 ml. Iron binding capacity 190 μg. iron/100 ml.

Fig. 2. *Cranium:* Photograph taken at autopsy after dome had been removed showing tumor on the roof of the right orbit and a mass invading and protruding at the sella turcica.

Roentgen Findings. 1955: There was extensive destruction of the cranial vault with marked thinning and destruction of the sella turcica and dorsum sellae. The pineal gland was calcified and in the midline. There was no evidence of a retrobulbar mass. The optic foramina showed no gross abnormalities. A right common carotid angiogram revealed

Fig. 3. *Sphenoid Sinus:* A section (×40) of the sphenoid sinus shows abrupt transition from normal epithelium on the right to frank tumor. Here the tumor cells show a hyperchromatic, vesicular nucleus, a moderate degree of cytoplasm and occasional prominent nucleoli.

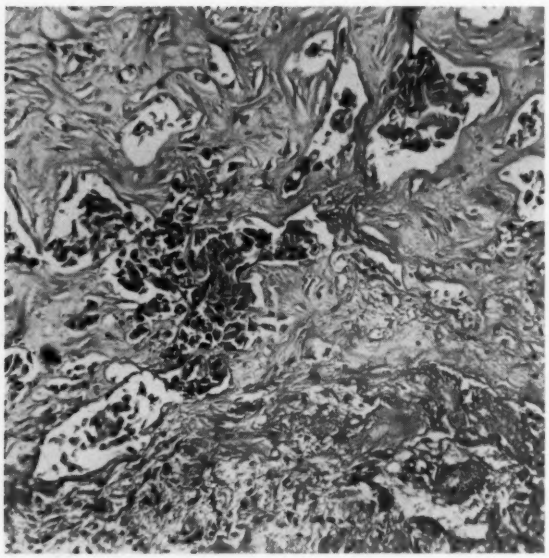

FIG. 4. *Sphenoid Sinus:* A section (×125) through the tumor mass in the sphenoid sinus shows clusters of epithelioid cells with a moderate degree of cytoplasm, a prominent vesicular nucleus and a few mitotic figures. These cells occur in a rather dense eosinophilic connective tissue stroma with clefts and varying size areas of hyalinization.

slight narrowing of the distal portion of the internal carotid artery, probably within normal limits. Roentgenogram of the left femur demonstrated a fracture of the mid-shaft with anterior bowing at the fracture site. Intravenous pyelography was within normal range.

Electroencephalographic Findings. December, 1954: There were generalized abnormalities indicating a diffuse involvement of the cortical and subcortical regions. February, 1955: A subcortical (posterior fossa) process was indicated. June, 1955: There was no change.

Consultations. December, 1954: Ophthalmoscopic examination revealed lenticular cataracts O.D., cortical O.S. and posterior subcapsular O.D.; arteriosclerosis of retinal and choroidal vessels O.D.; arcus senilis O.D.; questionable minimal stromal keratitis O.D. of unknown cause. February, 1955: Neurologic study showed progressive right cavernous syndrome with involvement of the oculomotor nerve, sixth nerve and second division of the fifth nerve; ptosis of the right lid; atrophy of the temporal side of the right disk. Two possibilities were considered: 1. an osteogenic sarcoma of the base of the skull and; 2. an extradural aneurysm in the mid-cavernous region. On April 6, 1955, percutaneous right carotid angiography was done and the findings were thought to be within normal limits.

Course. On April 9, 1955 though the patient had failed to respond to cortisone, it was decided to try meticortone and she received 40 mg. daily for one week without alleviation of her bone pain. The persistent head pain required narcotics for relief and the patient became tolerant to these drugs.

On May 19, 1955, a prefrontal leukotomy was performed. This gave her some relief although she still felt the pain in her head.

She returned home to Brant Lake, New York. Epistaxis developed and became a serious problem requiring packing of the nose. The severe headaches returned.

By 1954, vision had been lost in the right eye and in 1955 she became totally blind. The power to move the jaw was lost and it was impossible for her to chew or talk and she had difficulty in swallowing. She was admitted to a nursing home. She died on September 21, 1957.

An autopsy was performed at the Glens Falls Hospital.

Pertinent Autopsy Findings. At the time of autopsy the body was that of an emaciated, elderly female with gray hair whose right leg was shorter than the left leg (7 cm.). A well healed midline suprapubic scar was noted. There was

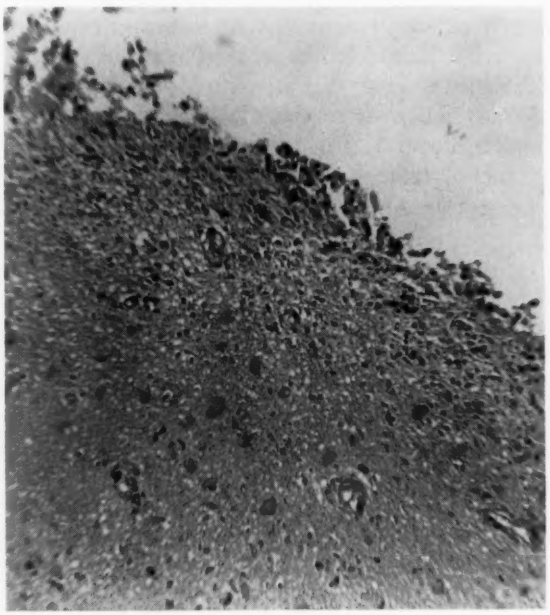

FIG. 5. *Brain:* A section (×125) of the under surface of the frontal lobe shows tumor extension into the cerebral stroma.

also a surgical scar, healed, on the upper third of the right thigh. The right eye was exophthalmic and it was impossible to close the eyelid over it. The corneae of both eyes were rather opaque and the conjunctivae were congested. In the frontal region two circular, slightly depressed areas, 3 cm. in diameter, were noted to the left and right of the midline. Examination of the head revealed the depressed areas to represent two roughly circular defects in the frontal bone which were covered on their external surface by the epicranial aponeurosis and on the inner surface by the dura. These defects measured 2 cm. on the right side and 2.5 cm. on the left. The bones of the cranium showed marked difference in thickness varying from 5 mm. to less than 1 mm. The sulci and gyri in the region of the frontal lobes showed shallowness and there was some flattening noted. On removal of the brain, a nodular gray-white, spherical, moderately firm tumor 4.5 cm. in diameter was noted which was overlying the second portion of the sphenoid bone and involved the sella turcica. The external surface of this tumor was smooth in places, slightly shaggy in others and was pearly gray. The pituitary gland had been displaced upward and laterally by the growth of tumor. It was 1.5 cm. in diameter, gray and smooth. The tumor was located to the right of the midline extending into the small wing of the sphenoid and the roof of the right orbit. The optic chiasm was partly embedded in the tumor. The tumor extended anteriorly overlying the cribriform plate and partly engulfed the crista galli. Tumor also extended along the right optic nerve through the optic foramen, involving the periocular tissues on the right, producing protrusion of the eye. An accessory spleen was noted.

Fig. 7. *Lower Extremities:* Roentgenogram taken in 1953, four years before death. The incomplete fracture of the femoral shaft is shown. The right femur has been shortened by the ununited fracture of the upper portion of the shaft. Many cystic are seen throughout the femoral shaft and a generalized demineralization is noted. Punctate calcifications suggest infarcts in the lower femoral shafts. The condyles of the femora and tibiae show marked bone condensation. A growth arrest line is seen in the right tibial condyles.

Fig. 6. *Pelvis:* Roentgenogram taken in 1953, four years before death. There are areas of rarefaction and coarse, irregular bone condensation. Both hip joints are almost completely ankylosed due to extensive osteoarthritis. The ossification centers for the iliac crests remain ununited.

The right femur on the upper third of the shaft showed a fragment of bone, 5 cm. × 3 cm., which had embedded within it two screws. On the cut surface this bone showed a number of varying sized spaces. The bony cortex varied in thickness from 5 mm. to areas where it was extremely thin.

Radium and Mesothorium Body Burden. Measurements on the cadaver by Dudley at Massachusetts Institute of Technology gave a radium content of 7.6 μc. The gamma determination was 6.6 ± 0.7 μc, the radium equivalent by radon 1.0 ± 0.5 μc. The mesothorium by gamma determination was less than 0.1 μc.[1]

FIG. 8. *Left Knee:* Roentgenogram taken in 1950, seven years before death. Areas of bone condensation and rarefaction are seen in the lower end of the femur in the upper tibia. Growth arrest lines are seen in the upper tibia and fibula. Cystic changes are seen in the tibial and fibular shafts.

A brief summary of the patient's history in chronologic order is given in Table 1.

DISCUSSION

Many thorough and painstaking studies are found in the literature which document the pathologic changes in the bones, viscera, and soft tissues of patients suffering from chronic radium poisoning. Blum[4] was the first to recognize osteomyelitis of the maxilla and mandible caused by radioactive materials deposited in the bones. In 1924, he read a paper on the subject before the American Society of Oral Surgeons and Exodontists describing a lesion called radium jaw which resembled phosphorus necrosis. Martland and his co-workers[18–21] made many contributions to the understanding of the subject. They performed autopsies on many of the dial painters and also on several of the scientists who prepared and measured out the material for the watch dials.

According to Martland and Humphries,[20] mesothorium formed 70 per cent of the radioactivity of the ingested material. Since the half-life of mesothorium is 6.7 years, the amount in the body decreased significantly as time passed.

Early measurements of the body burden were rather crude and not accurate, in the opinion of Aub, Evans, Hempelmann, and Martland.[2] Very sensitive physical techniques for measuring the total radium content of a living person were developed by Evans.[7] In 1943, he was routinely measuring the breath radon on all the personnel of nine dial painting plants in the eastern part of the United States.[8] This system of monitoring the workers proved to be a desirable safeguard. Hygienic working conditions and protective measures had been instituted by the companies, the licking of

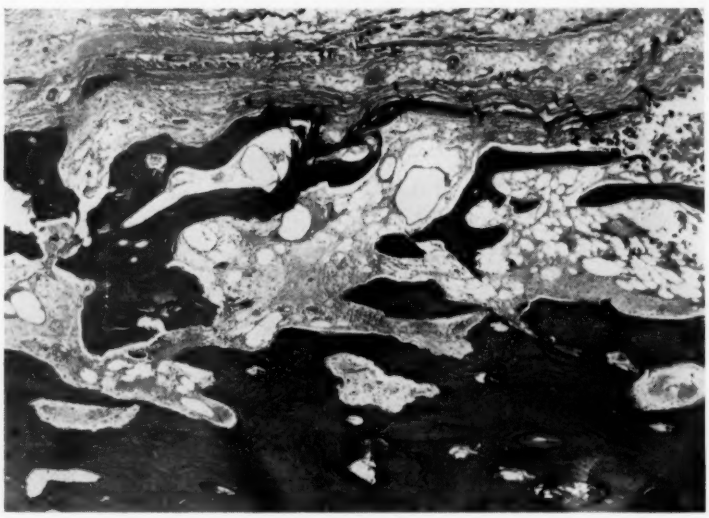

FIG. 9. *Right Femur:* Photomicrograph (×40) of a fragment shows areas of bone destruction and fibrous replacement of medullary structures. No evidence of tumor noted.

TABLE I

SUMMARY OF HISTORY

1917–1918	Radium and mesothorium ingested
1928	Fracture of right femur
1929	Refracture of right femur
1929	Body burden = 15 μg. of radium (Flinn)
1930	Fracture of femur plated
1931	Fracture of femur replated
1931	Left mastoiditis
1931	Jaw pain; teeth extracted
1935	Body burden = 3.9 μg. of radium (Flinn)
1937	Fracture of left femur; sequestrum of mandible
1940	Body burden = 8 μg. of radium (Flinn)
1941	Fracture of right clavicle
1945	Hysterectomy for leiomyomata
1952	Fracture of left clavicle
1953	Onset of severe headaches
1954	Body burden = 7.4 μg. of radium (radon), 8.0 μg. (by gamma radiation) (Looney)
1954	Refracture of left femur, lenticular cataracts
1954	Prefrontal leukotomy
1955	Total blindness
1956	Severe nasal hemorrhages
1957	Exophthalmos, loss of strength in jaw, inability to swallow
1957	Fracture of left scapula
1957	Died, September 21
1959	Body burden = 7.6 μc; cadaver measurements (Dudley)

brushes had been forbidden, and the dial painters seldom accumulated more than the tolerance for radium.

Roentgenographic changes in bones containing radium have been compared with the concentration of radium in given areas of these bones by means of autoradiography and the greatest bone destruction is not always in the area of highest concentration. Radium is not uniformly distributed in the skeleton. Autoradiographs of the bones of man and experimental animals have proved this point. The areas of highest concentration are not fixed. Some, or even all, of what has been deposited at one site may be mobilized in the course of time, and what is not excreted, may be redeposited at a new site of deposition or reconstruction. As Jaffe[13] points out, radioactive material tends to concentrate where osseous tissue is being laid down during bone growth or maintenance or during reconstruction in the course of metabolic wear and tear.

Martland[19] stated that alpha radiation accounts for 95 per cent of the damage to the body from the retained radioactive material. Rajewsky[25] also claimed that the biologic effect of the deposited materials is mainly due to alpha particles in contrast to the gamma radiation in ordinary radiation therapy. He stated that while the injuries produced in tissue by a gamma ray are extremely few per unit volume, those due to alpha particles are highly concentrated, and a cell can more readily recover when traversed by a gamma ray than when damaged by an alpha projectile. The alpha particle effect in tissues is completely cumulative, while the gamma ray effect is known to be in a large measure dependent on the recovery factor (protraction of dose).

One microgram of Ra^{226} forms 2.1×10^{-12} curies of Rn^{222} per second. Some of the radon, a rare gas, escapes from the site of formation and is eliminated in the exhaled breath, while the remainder disintegrates in the body and deposits other radioactive nuclides, some of which emit highly penetrating gamma rays.[26] An average of 70 per cent of the total radon produced in long-standing cases of radium retention is exhaled. The time of exposure to radium in chronologic time is of great importance in the prognosis of a given case.[23]

CONCLUSION

The radium and mesothorium which were permanently deposited in the skeleton produced weakness and brittleness of all the bones. This damage was caused by the internal emission of alpha particles. Since bone growth was proceeding at the time of deposition of the radioactive elements, when the patient was still seventeen, the epiphyseal plate areas showed extensive laying down of calcium.

Sarcomatous degeneration of bone which is the most common late effect of chronic radium poisoning did not develop in this patient although it was suspected to be

present after several pathologic fractures had occurred. A carcinoma which arose in the right sphenoidal sinus was probably a late effect of the prolonged radioactivity to which this patient's tissues were subjected.

SUMMARY

The case of a fifty-seven year old female, who was exposed to radioactive material for a period of fourteen months while working as a radium watch dial painter, is described. She survived thirty-nine years following exposure. During this period she suffered multiple pathologic fractures, osteomyelitis of the mandible, mastoiditis and a generalized radiation osteitis. She died of a carcinoma of the sphenoidal sinus which produced total blindness and accounted for the intractable headaches the last several years of her illness.

James A. Glenn, Jr., M.D.
206 Glen Street
Glens Falls, New York

We are indebted to Drs. Crawford Campbell, Benjamin Castleman, Sidney Farber, Hermann Lisco, C. Howard Hatcher, Arthur Stein and Shields Warren for assistance with and opinions of the slides. Dr. Jonathan Cohen had some excellent slides made which established the exact nature and origin of the tumor. The Presbyterian Hospital of New York City and Elliott and Ellis Bolton also provided many facts for the case history. Jack Masur, Director of the Clinical Center of the National Institutes of Health, made available a complete copy of the medical record. The photographs are presented through the efforts of Dr. Raymond Stokes, Robert H. and James A. Glenn. The photomicrographs were made by James A. Glenn. One of us (C.E.L.) was responsible for the opportunity of carrying on postmortem studies. We are also indebted to Miss Sue Whittemore for the secretarial work provided.

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THE TREATMENT OF INOPERABLE CANCER OF THE BILIARY SYSTEM WITH RADIOACTIVE (I^{131}) ROSE BENGAL*

By IRVING M. ARIEL, M.D., *and* GEORGE T. PACK, M.D.
NEW YORK, NEW YORK

ROSE bengal (nonradioactive), an organic dye, has been used as a test of liver function. This dye, when administered intravenously, is rapidly concentrated by the parenchymal liver cells which in turn secrete them with dispatch into the biliary system for excretion.

Recently, the stable iodine atoms have been replaced with radioactive iodine (I^{131}). Following intravenous injection, the gamma irradiation of the radioactive dye can be readily detected over the liver and the dynamics of the capacity of the liver to remove the dye from the blood stream and excrete it into the bile passages can be determined by using scintillation counting devices.

A number of reports on the use of radioactive iodinated rose bengal as a test of liver function have been published.

The normal isotopic hepatogram and the abnormalities resulting from certain pathologic states involving the liver are shown diagrammatically in Figure 1. It will be noted that if a scintillation counter is placed over the liver of a normal individual and the radioactivity measured, a peak is reached in approximately one hour, which peak then falls off so that by the end of twenty-four hours a preadministration level has been attained. In the case of parenchymal damage to the liver, the hepatic pick-up of the dye is diminished and its excretion delayed. In the case of extrahepatic biliary obstruction due to calculi, a lower peak is obtained (at times the peak may be delayed or abnormally low) and the excretion is markedly delayed.

Inasmuch as the dye containing the radioactive iodine is rapidly shunted from

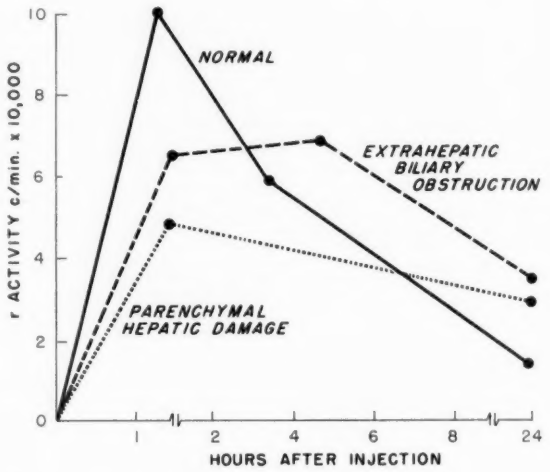

FIG. 1. Diagrammatic representation of the curves obtained by counting gamma activity over the liver following the intravenous administration of radioactive iodinated rose bengal. The curves for the major forms of hepatic derangement are illustrated.

the parenchymal liver cells into the biliary cells for excretion, it seemed plausible to investigate if neoplasms arising from the biliary system—whether intrahepatic or extrahepatic—would concentrate the dye in sufficient quantities to permit the irradiation from the gamma-emitting I^{131} to damage or destroy the cancer. Since most patients with cancer of the biliary system manifest evidence of biliary obstruction, an increased retention of administered radioactive iodinated rose bengal within the biliary system and, presumably, within the cancer would be anticipated.

This report describes clinical experiments in which the metabolism of the administered radioactive iodinated rose bengal was measured both in normal individuals and in patients with cancer of the biliary sys-

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tem. The clinical results of treating a series of patients bearing inoperable cancer with radioactive (I^{131}) rose bengal will be presented.

METHODS

Each patient was given the radioactive iodinated rose bengal intravenously by a remote control method (Fig. 2). Because rose bengal is rapidly excreted, an effort was made to saturate the excretory mechanism by administering a part of the radioactive isotope rapidly, after which the second half of the dose was administered over a period of three to five hours. It was hoped that this method of administration would permit increased retention of the isotope and, hence, irradiation of the biliary cancer for a more prolonged period.

The investigation was divided into two phases. In the first phase, 5 patients, who had had cholecystectomy with the insertion of a T tube into the gallbladder because of cholelithiasis, received from 500 μc to 5 mc of I^{131} rose bengal and excretion studies were performed to note the routes and rates of excretion of the radioactive iodinated rose bengal. One normal individual without external biliary drainage received 1 mc of I^{131} rose bengal. Repeated scanning over the liver region was performed in these patients to establish the isotopic hepatogram. Corporeal distribution and excretion of I^{131} were determined. Larger doses of I^{131} rose bengal were used in this study than the 5 μc usually reported for hepatic function tests in an effort to note the distribution pattern of a dose that more closely simulates the therapeutic doses.

The second phase of the study consisted of the intravenous administration of therapeutic doses of radioactive iodinated rose bengal to 14 patients bearing cancer of the biliary system (Table 1). Hepatic scanning and excretory studies of the routes and rates of excretion of the radioisotope combined with rose bengal were performed. Counting was made with an NRD Radimax sodium iodide crystal scintillation

Fig. 2. Demonstrating the intravenous administration of therapeutic doses of radioactive iodinated rose bengal by the remote control technique.

counter (manufactured by NRD, St. Louis, Missouri). These counters utilize the "plateau" of the photomultiplier without artificial voltage control in the counter. The efficiency for I^{131} is approximately 100 per cent. The aperture is three fourths of an inch in diameter and is shielded by lead. The counter was placed one and five eighths inches from the skin. The scaler used was an automatic Tracerlab SC-33 "1000" scaler. Scintigrams were performed over the hepatic region in 3 patients. In these instances, 250 μc of radioactive iodinated rose bengal was given intravenously and approximately twenty hours later this dose was repeated. Two hours after the administration of the second dose, a scintigram of the hepatic region was made, utilizing a highly shielded and collimated scintillation detector equipped with a gamma ray spectrometer. The authors are

Table I

CLINICAL FEATURES OF PATIENTS WITH CANCER OF THE BILIARY SYSTEM TREATED WITH RADIOACTIVE IODINATED ROSE BENGAL

Patient	Age and Sex	Symptoms	Duration of Symptoms before I^{131} Treatment (months)	Pathologic Diagnosis	Extent of Pathology	Previous Treatment	Dose and Date of I^{131} Rose Bengal	Results	Comment
N.S.	47 F.	Complete obstruction. Jaundice. Weight loss of 10 lbs. in 3 weeks	12	Adenocarcinoma of the common duct at level of cystic duct (mucin-producing)	Complete obstruction of common duct. Hydrops of the gallbladder	Exploratory laparotomy with excision of common duct 10-13-55. Exploratory laparotomy 4-20-56. Roentgen therapy 300 r daily for 3,000 r×2	11 mc 8-14-56	Died in 6 weeks	No benefit. Treatment given too late. No complications
L.D.	45 M.	Jaundice. Ascites. Weight loss	16	Carcinoma of the common and intrahepatic biliary ducts	Extensive metastases to liver	Exploratory laparotomy and rubber tube inserted into bile duct 10-25-55	11 mc 1-7-57 31 mc 1-31-57	Died in 2 months	No benefit. No complications
P.D.	40 M.	Obstruction. Jaundice. Weight loss of 30 lbs.	14	Adenocarcinoma of the common and hepatic ducts (anaplastic)	Almost complete obstruction of the ducts	Exploratory laparotomy 4-13-56	12 mc 8-23-56 10 mc 11-1-56	Died in 3 months	Mild palliation
F.F.	54 M.	Severe pruritus. Jaundice	12	Adenocarcinoma of the gallbladder	Complete obstruction of the common and hepatic ducts. Metastases to lymph nodes	Exploratory laparotomy 10-24-56	11 mc 11-12-56 11 mc 12-6-56	Died in 9 months. Pneumonia	Moderate palliation. Decrease in pruritus. Sense of well-being. No significant effect on longevity
M.G.	40 F.	Sense of mass. No other symptoms	12	Carcinoma of the bile duct	Extensive metastases to both liver lobes	Exploratory laparotomy 12-12-55	12 mc 10-15-56 22 mc 7-22-57	Condition excellent for 6 months, then liver began to enlarge Died in 22 months	Patient received roentgen therapy 7 months after rose bengal. Palliation
W.R.	53 M.	Jaundice. Abdominal pain	12	Adenocarcinoma of the common duct. Low grade malignancy	Carcinoma extended up both hepatic ducts	Exploratory laparotomy. Insertion of T-tube 7-3-57	22 mc 8-16-57 13 mc 12-19-57	Mild relief of symptoms Died in 11 months	Developed paresthesia of both feet. Spinal tap and roentgenogram of spine normal
K.K.	64 F.	Jaundice. Weight loss. Weakness	10	Adenocarcinoma of the common bile duct	Carcinoma extended down to invade ampulla and extended to liver	Exploratory laparotomy. Insertion of T-tube 9-13-57 Re-exploration and hepatojejunostomy and re-insertion of T-tube 2-26-58	18 mc 10-10-57 23 mc 12-2-57	Died in 5 months	No benefit. Liver did not pick up rose bengal. Question of hepatitis

TABLE I (*continued*)

Patient	Age and Sex	Symptoms	Duration of Symptoms before I^{131} Treatment (months)	Pathologic Diagnosis	Extent of Pathology	Previous Treatment	Dose and Date of I^{131} Rose Bengal	Results	Comment
C.H.	65 M.	Jaundice. Pruritus	10	Adenocarcinoma of the common bile duct	Carcinoma extended into liver	Exploratory laparotomy. Biopsy May, 1958	15 mc 7-13-58	Died in 5 months	Developed bilateral foot drop and loss of knee reflexes after rose bengal. Cause?
I.H.	54 M.	Jaundice. Weight loss. Weakness	48	Adenocarcinoma of the common bile duct. Low grade malignancy	Extension into liver and ampulla. Stones found in the gallbladder	Exploratory laparotomy. Insertion of T-tube April, 1956	10 mc 8-30-56 11 mc 11-19-56 26 mc 4-7-58 18 mc 9-8-58	Died in 24 months	Excellent palliation
A.G.	59 F.	Jaundice. Weakness	8	Carcinoma of the gallbladder	Carcinoma extended to both lobes of the liver	Exploratory laparotomy. Biopsy of liver 4-29-57	22 mc 5-17-57	Died in 1 month	No benefit. Given too late
E.W.	59 F.	Jaundice. Weakness	36	Carcinoma of the gallbladder	Carcinoma extension to liver	Exploratory laparotomy 5-14-58 Re-explored 8-1-58	15 mc 8-11-58	Died in 2 months	Early symptoms may have been due to biliary calculi. Postmortem examination showed severe cholangitis. Question as to whether due to rose bengal. No radiation changes in tumor
M.D.	45 F.	Abdominal mass. Weakness. Jaundice	12	Carcinoma of the gallbladder	Extension to liver	Exploratory laparotomy and cholecystectomy May, 1957. Roentgen therapy to metastases of lumbar vertebrae	20 mc 6-12-58	Well but weak 9 months later	Moderate relief of symptoms. No decrease in size of liver
J.W.	44 M.	Weakness	15	Carcinoma invading bile ducts. Question of primary	Extension to omentum, peritoneum and liver	Exploratory laparotomy and insertion of T-tube 9-14-56	10 mc 1-10-57	Died in 14 months	Questionable benefit because other palliative procedures had been instituted. No complications
I.H.	67 M.	Jaundice. Weight loss. Abdominal mass	12	Carcinoma of the gallbladder	Metastases to both lobes of the liver. Ascites	Exploratory laparotomy. Biopsy of liver June, 1958	20 mc 2-6-59 20 mc 4-10-59	Alive	Marked relief of tenderness in hepatic region

indebted to Dr. Joseph Greenberg of the Long Island Jewish Hospital, New Hyde Park, Long Island for performing the hepatic scintigrams presented in this report.

The I^{131} was administered as the sterile neutral solution of the sodium salt. The specific activity averaged 100 μc per mg. of dye. Loosely bound iodine was less than 2 per cent. The material has an iodine content of 8.15×10^{-6} mg./mc (0.00000815 mg./mc). The average concentration equalled 1–1.5 mc/ml. The average dose equalled 10–20 ml. of solution diluted by approximately 200 ml. of normal saline solution by the remote method of administration (Fig. 2). In view of the variation in the doses of I^{131} rose bengal given to the different patients in this study, the results are not suited for comparing the counts obtained from one patient to another. The data do permit an evaluation of the transport of the isotope in each of the patients investigated.

METABOLISM OF RADIOACTIVE IODINATED ROSE BENGAL

The fate of administered I^{131} rose bengal has been investigated by Taplin, Meredith, and Kade[12] and Lum, Marshall, Kozoll, and Meyer.[8] These authors indicated that in the normal individual rose bengal is rapidly cleared from the blood stream by the polygonal cells of the liver and passes quickly through the parenchymal liver cells into the biliary canaliculi, whence it is excreted into the intestinal tract. The reticuloendothelial system plays no role in this passage.

Cohen, Giansiracusa, Strait, Althausen, and Karg[3] have demonstrated that the blood clearance curves of rose bengal are almost identical to those of bromsulphalein in humans with normal hepatic function. In normal human beings, the clearance of administered rose bengal from the blood occurs with great rapidity. The peak of concentration of the administered dye in the liver usually occurs within an hour, after which there is a rapid fall-off as the efficient excretory mechanism rids the organism of the administered dye.

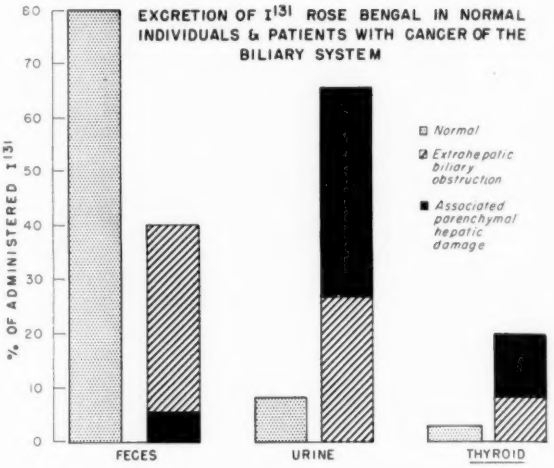

FIG. 3. Excretion of I^{131} rose bengal in normal individuals and in patients with cancer of the biliary system.

Defects in excretion occur in patients with extrahepatic biliary obstruction, and defects in concentration by the liver occur in patients with disease of the parenchymal hepatic cells (Fig. 3). These abnormalities of concentration and excretion of the dye, which form the basis of a rather sensitive test in patients with jaundice, play an important role in employing therapeutic amounts of radioactive iodinated rose bengal for patients with cancer of the biliary system.

A normal person will excrete the administered dye rapidly. Table II shows the biliary excretion of I^{131} rose bengal in a patient shortly after cholecystectomy for cholelithiasis and who received 1.2 mc of I^{131} rose bengal. It should be noted that a significant excretion in the bile occurred within one half hour after the administration and the peak occurred at one hour after the injection, after which there was a rapid fall-off in the excreted I^{131}. A similar curve (Table III) prevailed in a normal individual who had had an anastomosis of the bile duct and who was inadvertently given 5 mc of the radioactive iodinated rose bengal. (It had been planned to give her 500 μc.) In this case, the peak of ex-

cretion also occurred at one hour but a large amount of activity was detected in the excreted bile five hours after the injection, after which there was a rapid fall-off, but some activity was still present in the bile obtained through the T tube eighty-eight hours after the administration.

Table IV illustrates the routes of excretion of the radioactive iodinated rose bengal in a normal person. It reveals that the main excretory route is via the feces, with some being excreted by way of the urine. Because of collection difficulties, it was not possible to determine the total I^{131} excreted by way of the urine and in feces. The counts per milliliter do indicate the relative excretory pattern. The I^{131} noted in the feces is presumed to be attached to the rose bengal molecule. The nature of the urinary I^{131} cannot be determined from these studies. Whether it represents free iodide which has become detached from the rose bengal molecule or an organic io-

Table II

BILIARY EXCRETION OF RADIOACTIVE I^{131} ROSE BENGAL AFTER INTRAVENOUS ADMINISTRATION OF 1.2 MC

(normal)

Time of Collection after Injection (hours)	Total Amount of Bile (ml.)	Gamma C/min./1 ml. Bile	Gamma C/min./ Total Bile Excreted
0.5	28	2,316	64,848
1	15	168,855	10,131,300
1.5	3	173,765	251,295
5	10	83,558	835,580
9	15	7,607	114,105
13	40	1,048	41,920
17	30	282	8,460
21	58	94	5,452
25	29	82	2,378
29	23	62	1,426
33	No drainage		
37	No drainage		
41	2	72	72
45	No drainage		
49	35	43	1,505
53	4	65	262
57	2	70	70
61	.5	55	55
65	No drainage		
69	No drainage		
73	.5		
77	No drainage		

Table III

BILIARY EXCRETION OF RADIOACTIVE I^{131} ROSE BENGAL AFTER INTRAVENOUS ADMINISTRATION OF 5 MC

(normal)

Time of Collection after Injection (hours)	Total Amount of Bile (ml.)	Gamma C/min./1 ml. Bile	Gamma C/min./Total Bile Excreted
0.5	15	21,313	319,695
1	14	198,773	2,782,822
1.5	18	130,873	2,355,714
5	80	13,825	1,106,000
9	69	147	10,343
13	56	26	1,456
17	44	13	572
21	42	12	504
24	59	9	531
28	49	12	668
32	54	10	540
36	3	14	42
40	59	7	413
44	56	9	504
48	35	9	315
52	52	10	520
60	7	9	63
68	88	8	704
72	74	8	592
76	9	10	90
88	110	11	220

Table IV

EXCRETION OF I^{131} ROSE BENGAL AFTER INTRAVENOUS ADMINISTRATION OF 1 MC IN A PATIENT WITH NORMAL LIVER FUNCTION

Time after Injection (hours)	Urine	Feces	Blood
	Gamma C/min./ml.	Gamma C/min./ml.	Gamma C/min./ml.
0.5			71,765
1.0	98,540	2,294	7,560
2.0			4,624
3.0			3,457
4.0			3,000
24	47,188	170,969	644
48	2,341	210,018	454
72	1,365	480,071	341

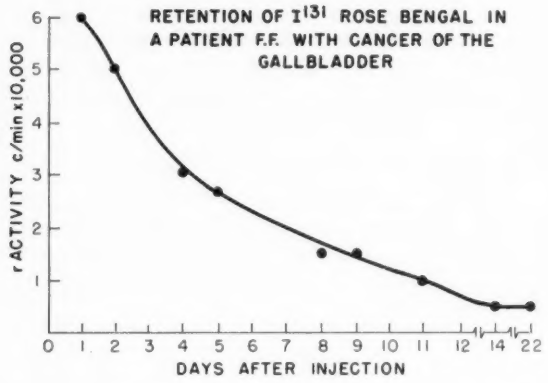
RETENTION OF I131 ROSE BENGAL IN A PATIENT F.F. WITH CANCER OF THE GALLBLADDER
r ACTIVITY c/min x10,000
6
5
4
3
2
1
0 1 2 3 4 5 6 7 8 9 10 11 12 14 22
DAYS AFTER INJECTION

Fig. 4. Retention of I^{131} rose bengal in a patient, F. F., with cancer of the gallbladder following the intravenous administration of 11 mc of I^{131} rose bengal. The counts were obtained over the site of the tumor.

dide could not be learned. That a slight amount of separation of the radioactive isotope from the rose bengal molecule does occur is suggested by a very slight increase of gamma activity over the thyroid region, even in the normal individual.

Patients with biliary cancer demonstrate abnormalities in the metabolism of the administered isotopic dye. Our findings are similar to those described by Lum, Marshall, Kozoll, and Meyer[8] for patients with carcinomatous obstruction of the bile ducts. Table v shows the excretion of iodinated rose bengal in a patient (I.H.) with cancer of the common bile duct who had external biliary drainage through a T tube. A significant quantity of the isotopic dye was excreted by way of the biliary system but very little, as would be expected, was detected in the feces. A great amount was excreted in the urine, and gamma activity was noted in the blood in significant quantities for approximately one week after the injection. Following a second injection of the isotope, at which time the T tube was clamped, very little was again excreted by way of the feces and great quantities were excreted by the urine. These observations indicate that a block of the normal excretory pattern existed, with the administered isotope being shunted into the systemic circulation for renal excretion. The exact nature of the mechanism of reabsorption or the state of the metabolite awaits elucidation. A similar phenomenon occurred in 2 patients with cancer of the gallbladder without external biliary drainage (Table vi), in whom there was a persistent and prolonged urinary excretion of the radioactive iodine. Neither of these patients had severe parenchymal disease as determined by liver profile studies.

Table V

THE EXCRETION OF I^{131} ROSE BENGAL IN A PATIENT WITH CANCER OF THE BILIARY TRACT AND T TUBE BILIARY DRAINAGE

Patient and Dose I^{131}	Day after Injection	Bile		Urine		Feces	Blood
		Quantity (ml.)	Gamma C/min./ Total Quantity	Quantity (ml.)	Gamma C/min./ Total Quantity	Gamma C/min./ml.	Gamma C/min./ml.
I.H. 10 mc	1	—	—	—	—	—	90
	5	168	39,144	690	26,220	33	16
	6	38	2,992	500	13,500	173	18
	7	164	28,864	655	15,720	211	10
	11	—	—	1,200	6,000	—	7
	18	—	—	880	2,640	—	2
Second Injection 11 mc	1	—	—	258	387,000	5	28
	4	—	—	1,505	13,545	307	—
	7	—	—	1,525	4,575	26	3

TABLE VI

THE EXCRETION OF I^{131} ROSE BENGAL IN 2 PATIENTS WITH CANCER OF THE BILIARY TRACT WITHOUT EXTERNAL BILIARY DRAINAGE

Patient and Dose of I^{131}	Day after Injection	Urine		Feces	Blood
		Quantity (ml.)	Gamma C/min./ Total Quantity	Gamma C/min./ml.	Gamma C/min./ml.
F.F. 11 mc	1	1,125	591,750	69	823
	3	2,310	2,811,270	34	171
	4	1,590	497,670	40	144
	7	1,950	261,300	7	74
	14	1,080	106,120	2	44
Second Injection 11 mc	1	2,070	78,942,160	380	16,105
	4	1,530	51,971,040	2,756	10,405
	5	1,410	39,506,480	6,405	9,407
	7	1,980	27,733,760	2,680	7,881
	8	900	20,712,600	791	7,132
	11	750	11,314,500	1,810	5,496
	14	900	9,151,200	1,493	2,578
	22	1,140	4,326,300	231	3,002
L.D. 10 mc	1	1,000	23,009,000	4,230	63,432
	3	500	7,068,000	1,430	6,758
	4	500	4,261,000	1,150	18,084
	7	750	1,662,750	800	1,755
	14	750	201,000	—	743

The corporeal distribution of the retained isotope is recorded in Tables VII and VIII. It may be noted that after the first injection, a significant quantity of gamma activity could be detected over the site of the cancer after a period of five days, after which there was a decrease. The rate of the decrease varied. The retention of the dye at the site of the tumor was more marked after the second injection in both patients. The pretibial site was surveyed for its gamma activity as a point of reference. A significant finding was the activity over the thyroid gland, particularly in patient F. F. (Table VIII). It should be noted that the activity increased with the passage of time, with the peak being reached seven days after the first injection and eleven days after the second injection.

These data demonstrate that, if a block occurs in the hepatic route for excretion of the radioactive iodinated rose bengal, the alternate route for excretion—*i.e.*, by way

TABLE VII

CORPOREAL DISTRIBUTION OF I^{131} ROSE BENGAL IN A PATIENT (I.H.) WITH CANCER OF THE COMMON BILE DUCT

Time after Injection (days)	Gamma C/min. over Tumor Site	Gamma C/min. over Spleen	Gamma C/min. over Thyroid	Gamma C/min. over Pretibial Site
First Injection—10 mc I^{131}				
1	5,100	1,576	—	180
5	3,700	2,200	—	24
6	860	600	—	12
7	70	47	—	0
18	25	10	10	0
Second Injection—11 mc 3 Months after First Injection				
0.5 hr.	5,700	1,000	100	10
1	1,170	500	730	8
4	1,000	90	420	0
7	1,750	25	100	0

TABLE VIII

CORPOREAL DISTRIBUTION OF I^{131} ROSE BENGAL IN A PATIENT (F.F.) WITH CANCER OF THE GALLBLADDER

Time after Injection (days)	Gamma C/min. over Tumor Site	Gamma C/min. over Spleen	Gamma C/min. over Thyroid	Gamma C/min. over Pretibial Site
First Injection—11 mc I^{131}				
1 hr.	5,000	2,900	1,190	150
1	3,650	1,070	1,110	130
3	1,630	810	1,112	110
4	1,400	610	1,500	90
7	620	40	1,950	60
14	80	50	380	0
Second Injection—11 mc 3 Weeks after First Injection				
2 hr.	600,000	480,000	104,000	17,000
1	503,000	206,000	90,000	16,600
4	245,000	77,600	78,000	11,700
5	193,000	66,000	79,000	9,000
7	106,000	33,000	78,800	4,800
8	98,000	33,000	72,000	4,700
11	60,000	15,900	447,600	2,800
14	33,000	14,000	95,800	1,800
22	10,000	3,400	6,000	700

of the urine—is not efficient, and retention of the administered isotope for a prolonged period occurs. A certain amount of I^{131} presumably separates from the dye, which is then concentrated by the thyroid gland in significant quantities. No evidence of hypothyroidism was observed in any of our patients but the effects of irradiation to the thyroid gland are a reality in such instances.

The reason why the counts after the second injection of 11 mc of radioactive iodinated rose bengal in patient F. F. (Table VIII) were so high cannot be stated. Whether they represent actual severe retention of the administered isotope or some quirk in the counting equipment cannot be determined. The data following the particular injection under review are consistent and can be used for determining the metabolic pathways of the administrated I^{131} rose bengal.

In instances of extrahepatic biliary obstruction, if the polygonal liver cells concentrate the administered radioactive isotope but its excretion is blocked, the liver cells—including the biliary cells and, presumably, the tumor arising from the biliary cells—will be subjected to prolonged irradiation. The desired effects of the irradiation upon the tumor in such instances must be counterbalanced against the possibly detrimental effects of the irradiation upon the liver.

It is difficult from these studies to determine the selective radiation effects upon the liver. That they were not severe is suggested by hepatic function tests of patient F. F. Obstruction persisted throughout his postisotopic period. His alkaline phosphatase, which was 36.4 S.J.R. units, dropped only to 29.9 S.J.R. units, and his serum bilirubin, which had been 21.8 mg. per cent, gradually increased to 77 mg. per cent and then decreased to 49 mg. per cent. The test of hepatic parenchymal function remained relatively normal throughout. The cephalin flocculation test was persistently negative; the thymol turbidity was always less than 5 units; and the cholinesterase averaged 0.5 pH units. The blood transaminase, however, did increase from 88 Beckman units to 177 Beckman units. The hepatic function tests in another case, patient I.H., are given in Table IX.

TUMOR SCINTISCANNING

Whether all tumors arising from the biliary system concentrate the radioactive iodinated rose bengal in significant quantities cannot be answered. Scintiscanning of the hepatic region with an automatic scintillation scintiscanner was performed in 3 patients by Dr. Joseph Greenberg. In each, the concentration of the I^{131} differed. The scintigram of patient W. R. (Fig. 5) is considered to be that of a normal liver and it is interpreted that the tumor of this patient did not effectively concentrate the

TABLE IX

HEPATIC FUNCTION TESTS IN A PATIENT (I.H.) WITH CANCER OF THE COMMON BILE DUCT DURING TREATMENT WITH RADIOACTIVE IODINATED ROSE BENGAL

	9-5-56	9-24-56	11-15-56	8-6-57	8-12-57	9-19-57	12-30-57	2-3-58	4-7-58	4-22-58	6-5-58	8-14-58	8-19-58	9-30-58	10-7-58
Chlorides (mEq.)												102			
Urea Nitrogen (mg.%)							11								14
Phosphorus (inorganic) (mg.%)	3.5	4.2	3.8	2.6		3.5			3.4	3.7	3.7				
Alkaline Phosphatase (S.J.R. units)	18.5	22.0	29.4	24.2		27.2	15		24.4	46.3	29.7	18.0			
Bilirubin (mg.%)	4.6	3.8	0.8	0.8			0.2		0.9	1.5	1.2	1.2		16.0	
Cephalin Flocculation (units)	2+	negative	negative	negative		negative		0.3	negative		negative				
Cholesterol (mg.%)	200	340	322	179	135			2+	142						
Esters (% total)	110	223	238		78				88						
Thymol Turbidity (units)	<5	<5	<5	<5											
Total Protein (gm.%)	67	8.0	6.4	6.6	6.4										
Albumin (gm.%)	3.9	4.8	3.6		3.0							5.5	7.2		
Globulin (gm.%)	2.8	3.2	2.8		2.4										
Cholinesterase (pH units)			0.58	0.61											
Transaminase (Beckman units)				96											

administered radioactive isotope. The scintigram of patient K. K. is remarkable in that none of the administered radioactive isotope was detected within the liver (Fig. 6*A*). The fact that this was due to actual failure of the liver to concentrate the dye and not to any defects in the scanning equipment is shown by the similar scintigram obtained from a biopsy of the right lobe of the liver four hours after the initial scintigram. A scintigram of this piece of liver *in vitro* also failed to reveal any pick-up of the previously administered isotope (Fig. 6*B*). Inasmuch as this absolute failure of ability to concentrate the dye by the liver has not been reported either in animals with induced severe liver damage or in humans with severe hepatitis, the exact cause for the observed response is unknown. The fact that this patient had taken thorazine introduces the possibility that her hepatitis was thorazine induced. Lum, Marshall, Kozoll, and Meyer[8] report that 3 patients with cholestatic jaundice associated with intrahepatic obstruction presented findings similar to patients with viral hepatitis. The uptake and excretion of the I^{131} rose bengal were slightly less than observed in normal individuals.

In the third scintigram, patient I. H., (Fig. 7) there was a heavy concentration of the administered radioisotope in a region where a large tumefaction could be palpated and at a site where the patient had complained of marked tenderness. It is interpreted that this represents a concentration of the dye by a large hepatic metastasis. It is suggested that when a patient with cholangiocarcinoma is considered to be a candidate for radioactive iodinated rose bengal therapy, a hepatic scintigram be performed to note the ability of the cancer to concentrate the administered radioisotope.

RESULTS OF TREATMENT

Effect on Longevity. Fourteen patients were treated with therapeutic doses of radioactive iodinated rose bengal. The initial dose was usually 10 to 20 mc; in a

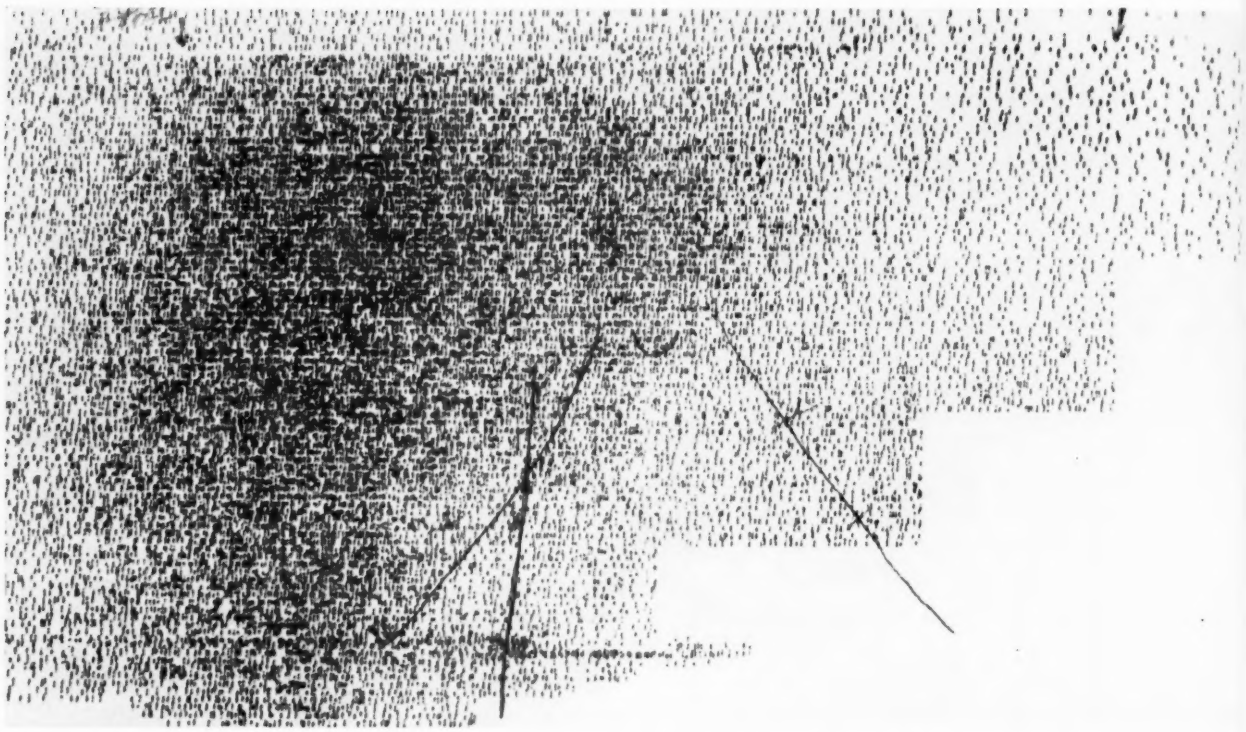

Fig. 5. Scintigram of the liver of patient W. R. with a carcinoma of the common duct. This is considered a scintigram of a normal liver.

number of patients this dose was repeated. Patient I. H. received four doses of the isotope for a total of 65 mc of radioactive iodine.

Of the 14 patients, 12 have died as the result of their cancer. The average duration of life of those who have died was eight months; the duration varied from six weeks to twenty-four months. It will be noted from Table 1 that a number of patients died less than two months after the administration of the radioactive isotope while others lived for prolonged periods. Thus, one patient lived for twenty-two months after the treatment and another for two years.

A clinical impression gleaned from observing the patients who lived for prolonged periods was that the beneficial effects were not of long duration. Thus, patient M. G., who had an excellent clinical response from the systemic administration of radioactive iodinated rose bengal, enjoyed the beneficial effect for a period of six months. During this six-month span, she was asymptomatic, engaged in all activities, and there was no demonstrable increase in the size of the hepatic mass. After six months, the liver began to enlarge and the patient complained of the sensation of a mass distending her abdomen.

The observation that all of these patients were given the isotopic treatment late in the course of their disease would suggest an advanced extent of the cancer. Practically all of the patients were treated at least ten months after the onset of their symptoms. In those instances where exploratory laparotomies were performed, marked invasion of contiguous structures, including extensive involvement of the liver, was usually observed, which would preclude an anticipated marked increase in longevity.

The average duration of life in most patients with inoperable cancer of the gallbladder and biliary ducts is approximately one year,[15] which would suggest that the

patients in this series received their course of radioactive iodinated rose bengal close to the end of their anticipated life span. Such was the case with patients N. S., L. D., P. D. and A. G., who died shortly after the administration of the isotope.

In this series were 7 patients with cancer of the common bile duct, 5 patients with cancer of the gallbladder, one patient with cancer arising from the intrahepatic bile ducts, and one patient whose bile ducts were involved by cancer but the exact site of origin could not be determined. There was no significant difference in the effect on longevity in these various groups. The average duration of life in the 7 patients with cancer of the common bile duct was seven months. Of the 5 patients with cancer of the gallbladder, 2 are alive—one nine months and the other one month after treatment. The average duration of life of the 3 patients with cancer of the gallbladder who succumbed was four months. The patient with cancer of the intrahepatic bile ducts survived twenty-two months after her radioactive isotopic therapy.

Palliative Effects. Patients who were in the most advanced stages of the disease usually had no benefit from the administered radioactive iodinated rose bengal

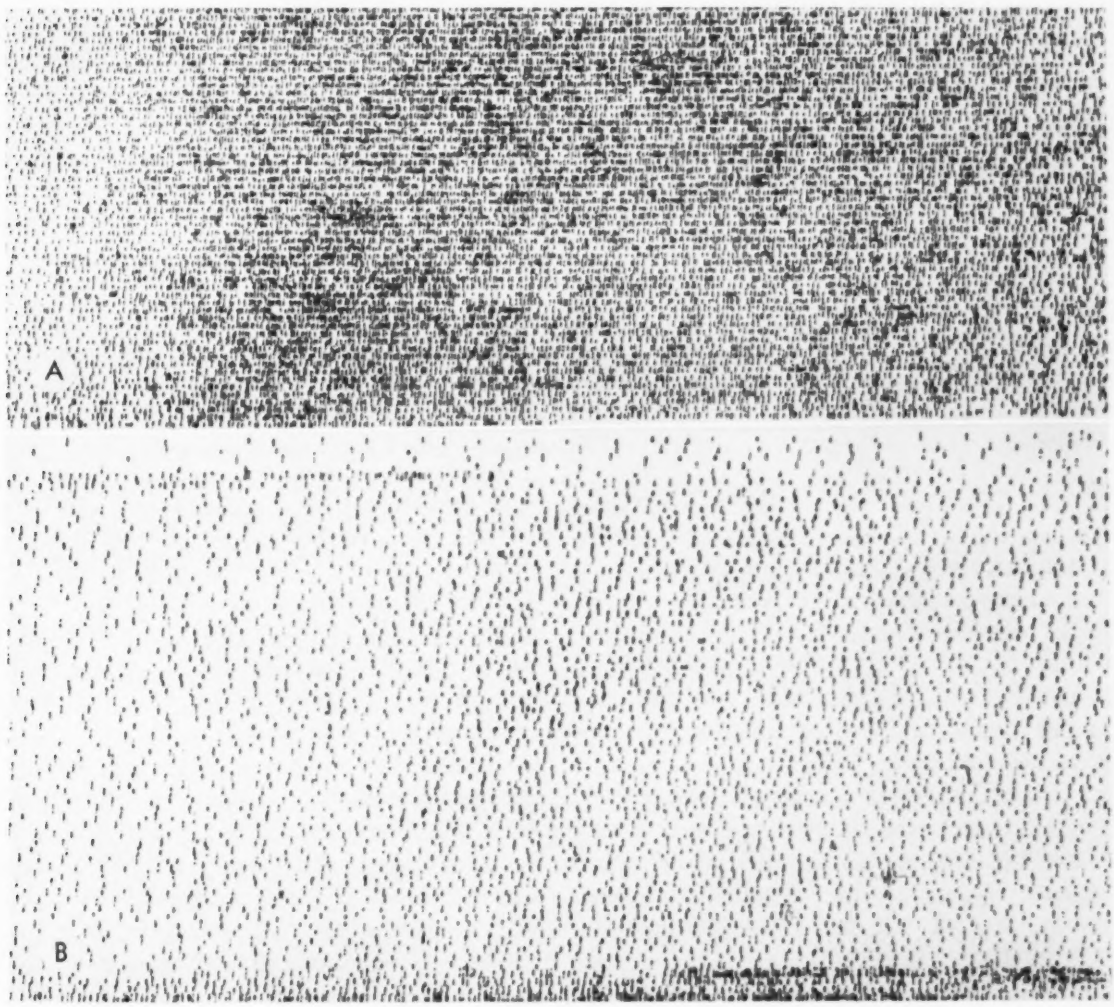

FIG. 6. (*A*) Scintigram of patient K. K. demonstrating almost complete failure of the liver to concentrate I^{131} rose bengal. (*B*) Scintigram of a biopsied portion of the liver of patient K. K. demonstrating no pickup of the I^{131} rose bengal by the liver.

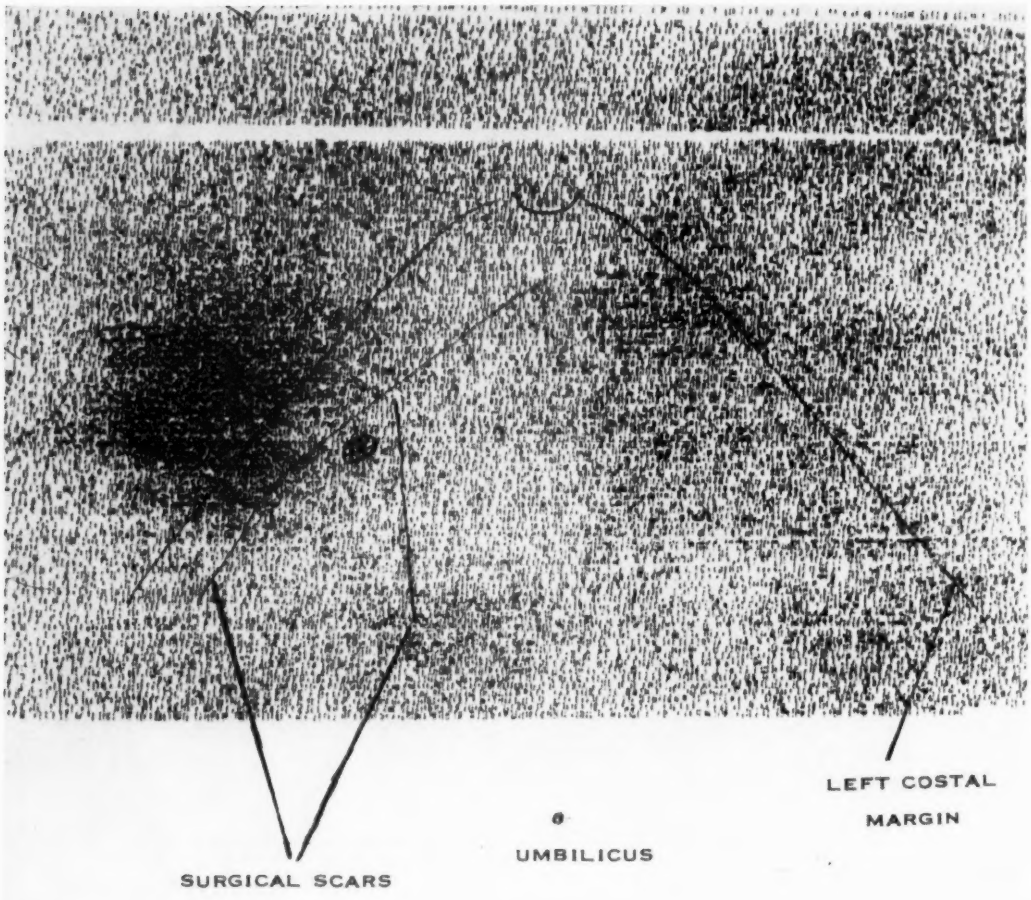

Fig. 7. Scintigram of patient I. H. showing the heavy concentration of I^{131} rose bengal at a site where a large tumor mass could be palpated and which site was exquisitely tender.

Five patients received no objective or subjective beneficial results from the administered isotope. Some degree of palliation was experienced by 9 patients. The beneficial effects consisted of a sense of well-being, improved appetite, and usually a gain in weight. In 3 patients a diminution in the degree of jaundice occurred; in one of these, there was a marked decrease of a severe, persistent pruritus, and in 2 others a diminution in the degree of bilirubinemia. Three patients noted relief of the tenderness in the hepatic region which had been present before the administration of the isotopic dye.

One patient, I. H., enjoyed excellent palliation following the administration of 10 mc of radioactive iodinated rose bengal. This patient was able to keep clamped a T tube which had been inserted in his biliary system into the tumor. After two months, however, signs of obstruction developed and it was necessary to release the clamp on the T tube (Fig. 8, *A* and *B*). A second dose of 11 mc of radioactive iodinated rose bengal was effective in that the T tube again could be clamped without clinical evidence of obstruction and the patient was asymptomatic. A third dose of irradiation was given almost two years after the first dose, again with a palliative effect but not as marked as with the first two courses of radioactive iodinated rose bengal, even though a much larger dose was given (26 mc of I^{131}). The patient eventually died from gastrointestinal hemorrhage after the tumor had infiltrated and eroded the duodenum.

COMPLICATIONS

One patient developed a bilateral foot drop after the rose bengal treatment. Another developed paresthesias of both feet, which a neurologist believed to be due to a lesion of the cauda equina but roentgenograms and scintigrams of this region after the administration of rose bengal failed to reveal any such lesion. Whether these neurologic conditions were the result of administered radioactive iodinated rose bengal cannot be stated. The dose of I^{131} (10 to 20 mc) and the dose of rose bengal (nonradioactive) were far below any toxic levels.

No effect upon the hematopoietic system that could be attributed to the isotope was observed. Although an anemia was present in many of the patients, involvement of the liver by the cancer was probably the causal factor. Each of these patients manifested a leukocytosis.

A postmortem examination of patient E. W., performed two months after the intravenous administration of 15 mc of radioactive iodine, was reported to reveal moderate cholangitis. No radiation changes were noted in the tumor or parenchymal organs of this patient. Postmortem examination of two other patients did not reveal any evidence of radiation effects upon the normal organs which could be attributed to the isotope.

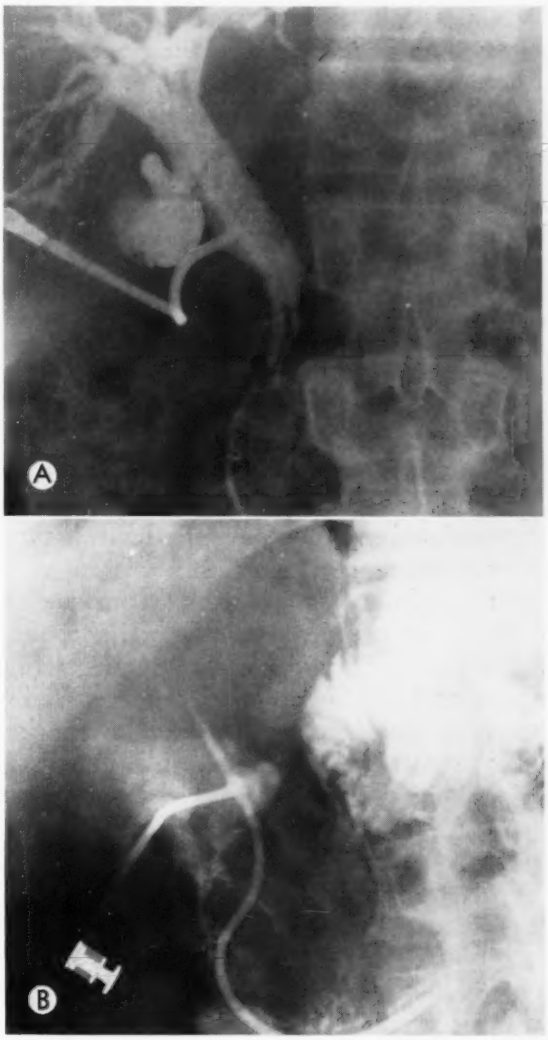

Fig. 8. (*A*) Postoperative cholangiogram illustrating the marked back pressure resulting from obstruction due to cholangiocarcinoma in patient I. H. (*B*) Cholangiogram taken subsequent to the administration of I^{131} rose bengal demonstrates the free flow of the radiopaque solution.

DISCUSSION

The systemic administration of radioactive isotopes to be concentrated selectively by a cancer has been a long desired goal. The ability of certain thyroid cancers to concentrate selectively radioactive iodine and thereby to be destroyed by the resultant concentrated irradiation has been well established. Radioactive phosphorus, administered systemically, has likewise been effective in irradiating patients with polycythemia vera and certain leukemias.

The systemic administration of radioactive isotopes, however, has yielded rather disappointing results for effectively irradiating most forms of solid cancer. Efforts to modify the chemical characteristics of a radioactive isotope by combining the isotope with an organic matrix are being investigated. The use of chelated yttrium for treating multiple myeloma[6] and of radioactive iodinated serum albumin for detecting brain neoplasms are samples of this type of experiment.[5]

The ease with which radioactive iodine can replace the stable iodine atoms of the rose bengal molecule (the potassium salt of tetraiodo-tetrachlor-fluorescein) and the

use of this radioactive dye as a test for liver function warrant its investigation as a therapeutic modality for effectively irradiating neoplasms arising from the biliary system—either intrahepatic canaliculi, extrahepatic bile ducts, or even the gallbladder itself. Experiments designed to study both the metabolism of the administered radioactive iodinated rose bengal and the clinical response of patients afflicted with inoperable cancer of the biliary system reveal that some cancers arising from the biliary system do concentrate the administered radioactive dye in significant quantities. Others do not.

The fact that obstruction to the biliary flow exists in many patients with this type of cancer, and obstruction leads to a retention of the dye, at times far prolonged, with a resultant irradiation of other organs such as the normal liver, the normal bile duct, and the intravascular elements, introduces an important factor for caution in the attempted treatment of patients with biliary cancer by the systemic isotopic route. The irradiation to the thyroid gland by radioactive iodine atoms which apparently separate from the rose bengal molecule is another feature that must be carefully observed. In addition, during the excretion of the radioactive isotope through the intestinal tract, the possibility of irradiation to the intestines must be considered.

The observations of the experiments herein reported reveal no untoward effects from the administration of the radioactive iodinated rose bengal. No instance of hypothyroidism was detected; no intestinal symptoms were complained of by the patients which might suggest possible intestinal irradiation; and there were no effects either upon the hematologic elements or liver function tests which could be considered an adverse reaction to the administered radioactive isotope. Many of these patients were critically ill and presented evidence of hepatic dysfunction and anemia, but in none were these abnormalities worsened by the systemic administration of the radioactive iodinated rose bengal.

One normal individual who had had an anastomosis of her bile duct to the right and left hepatic ducts was inadvertently given 5 mc of the radioactive iodinated rose bengal instead of a proposed 500 μc. This dose produced no demonstrable change whatsoever, and no effect upon the blood count and apparently no detriment to the healing of the anastomosis. Approximately 90 per cent of the administered dye was excreted through an indwelling T tube within forty-eight hours of its injection.

Postmortem examination of 3 patients who had received the radioactive isotope did not reveal any parenchymal damage that could be considered the result of the irradiation. In one instance, however, a cholangitis was considered by the pathologist to be secondary to the excretion of the radioactive material.

The clinical response of this group of patients varied from no response whatsoever to a marked relief of symptoms and an apparently increased longevity in others. As a rule, patients in a far-advanced stage of carcinomatosis did not respond to the treatment, and its use in such instances is not recommended. It may be stated, however, that even in these individuals the administration of from 10 to 20 mc of radioactive iodinated rose bengal did not produce any undesirable effects such as anemia, radiation sickness, etc.

A significant number of patients experienced relief from bothersome symptoms, sometimes to a remarkable degree. These patients enjoyed a sense of well-being, increased appetite, relief of pain and tenderness over the hepatic region, and sometimes the biliary obstruction relented.

Little can be said as to whether treatment increases the life span of the patient. It was our distinct impression that it did in at least 3 instances. Patient F. F., who was critically ill and appeared to be preterminal when first given the radioactive iodinated rose bengal, improved to a marked degree but died nine months later

from pneumonia. Patient M. G. died twenty-two months after the administration of the isotope; and the fact that her mass remained stationary in size for six months after the radioactive rose bengal therapy, after which it rapidly increased, is interpreted to reflect a restricting influence on the tumor, the result of the isotopic therapy. Patient I. H. lived for twenty-four months after his initial radioactive iodinated rose bengal therapy, with marked relief of symptoms during the major portion of his last years of life.

It is realized that certain patients with biliary obstruction can live comfortably with the simple institution of biliary drainage; but the ease of administration of rather large doses of radiation by the technique herein described, the beneficial response manifested by some of the patients herein reported, and the absence of untoward reactions as the result of such therapy would seem to make this a worthwhile form of treatment for certain patients with inoperable cancer of the biliary system.

The scintigrams of 3 patients with biliary cancer reveal that in one patient the cancer apparently concentrated the administered radioactive isotope to a significant degree. This patient also enjoyed marked clinical improvement following the isotopic therapy. Another patient, with hepatic metastasis from a carcinoma of the common bile duct, manifested no significant concentration of the radioactive isotope by the cancer. The reason for the differences in response cannot be commented upon. Both patients had adenocarcinomas of the common bile duct reported by the pathologist to be of "low-grade malignancy." The patient whose cancer concentrated the isotope lived for two years after the initial radioactive iodinated rose bengal treatment, in contrast to patient W. R. whose tumor apparently did not concentrate the dye and who died eleven months after the initial isotopic treatment, with but mild palliation. The liver of a third patient, afflicted with hepatitis of unknown etiology, could not clear the radioactive iodinated rose bengal from the blood stream. It is obvious that the administered isotope would not reach the cancer in such instances. These observations would suggest that scintigrams be obtained when possible, to determine the cancer's ability to concentrate the administered radioactive isotope.

If it is not possible to perform scintigraphy, and in view of the observations of the patients in this series none of whom showed clinical evidence of untoward radiation effects (except one who developed bilateral foot drop and another who developed paresthesias of the feet, possibly related to the therapy), a course of systemic radioactive iodinated rose bengal therapy in the dose range described could be used with relative safety.

The use of this type of therapy is contraindicated in any patient with severe parenchymal dysfunction of the liver. None of the patients in this series suffered from cirrhosis, and whether cirrhosis would contraindicate the use of this form of therapy is not known, but it is highly probable that the additional irradiation to the already damaged liver would be a detriment.

The vagaries of the concentration and excretion of the radioactive rose bengal by the cancer precludes an estimation of the total dose of radiation.

Irving M. Ariel, M.D.
139 E. 36th Street
New York 16, New York

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QUANTITATIVE EFFECT OF IODINATED OPAQUE MEDIA ON THYROIDAL UPTAKE OF RADIOIODINE*

By CHING TSENG TENG, M.D., *and*
JEAN KARAMOURTJOUNIS, M.D.†
HOUSTON, TEXAS

THE thyroidal uptake of a tracer dose of radioiodine as a test of thyroid function has in recent years superseded the basal metabolic rate and serum protein bound iodine determinations. This popularity is justified because of the relative simplicity of the procedure and the high degree of accuracy of the result in most instances.

An amazing number of factors, however, may affect some phase of thyroid physiology and iodine metabolism. Of these factors, iodine in any form, ingested or otherwise absorbed by the patient, will interfere with radioiodine uptake for a varying length of time and invalidate the results as an index of thyroid function.[2,3,8]

The organic iodinated compounds used as contrast media in roentgen diagnostic procedures have been reported to cause marked and prolonged lowering of radioiodine uptake.[2,3,8] Information with regard to the exact extent and duration of such effects, however, is rather meager in the literature.

A quantitative study of the effect of the iodinated opaque media used in cholecystography, intravenous pyelography, angiography, bronchography and myelography upon the uptake of radioiodine by the thyroid gland has been carried out. This report deals with serial observations before and after such contrast roentgen examinations. It was found that the effect was prompt, profound, and persistent and that recovery was gradual. The mechanism and practical implications will be discussed.

MATERIAL AND METHOD

The Selection of Patients. Hospital and clinic patients between twenty-six to sixty-nine years of age scheduled for cholecystography, intravenous pyelography, angiography, bronchography and myelography were selected for the study. The criteria for selection were (a) the patient exhibited no clinical evidence of thyroid dysfunction, and (b) there was no history of roentgenographic examination using an iodinated opaque medium in the past six months.

The Opaque Media. The iodinated opaque media used in our hospital, their iodine concentration, and the average amounts employed in the roentgenographic studies are summarized in Table 1.

The Procedure. Instead of the twenty-four hour thyroidal uptake, we have elected to determine the thyroidal uptake at the end of two hours following intravenous injection of a tracer dose. This was done primarily for the convenience of the patients. It was easier to secure their cooperation. It was also easier to be consistent in serial studies. A control uptake study was done before the roentgenographic examination with iodinated opaque medium; the uptake study was then repeated as frequently and as long as the patient was available until the result returned to his own control level.

The tracer dose of radioiodine was approximately 1 μc for the initial study and gradually increased to about 5 μc in follow-up studies as the radioactivity in the thyroid gland accumulated from previous studies increased. The maximum amount of the tracer dose received by any one patient did not exceed 40 μc.

These tracer doses were prepared in the departmental laboratory. An identical dose was used as a reference dose. The bottled

* From the Department of Radiology, Baylor University College of Medicine and Jefferson Davis Hospital, Houston, Texas.
† Visiting Scholar sponsored by the International Cooperative Administration. Present address: 36A Solonos Street, Athens, Greece.

Table I

Study	Opaque Media	Iodine Concentration	Amount Used
Cholecystography	telepaque	66.68%	6–12 tablets
Intravenous Pyelography	urokon 30% hypaque 50%	65.8% 59.87%	30 cc. 20 cc.
Angiography	urokon 30% hypaque 50%	65.8% 59.87%	20–50 cc.
Bronchography	dionosil oily	34%	10–20 cc.
Myelography	pantopaque	30.5%	6–9 cc.

doses were placed in a wax phantom and counted; counting rates varying within ±2 per cent were considered acceptable.

A thallium activated sodium iodide scintillation detector was used at a constant distance of 20 cm. The equipment was checked daily with a reference standard.

The thyroid area and the thigh were counted before and two hours after the intravenous injection of the tracer dose of radioiodine. The final count at each site was corrected by subtracting the pre-count. The reference dose was counted in a wax phantom which simulates the neck in size. The counting rate was corrected for the laboratory background count.

$$\% \text{ uptake} = \frac{\text{corrected thyroid count} - \text{corrected thigh count}}{\text{corrected reference dose count}} \times 100.$$

RESULTS

NORMAL CONTROL

Three patients who were in euthyroid state and had no history of iodine medication of any form have been subjects of ten serial two-hour radioiodine uptake studies within fifteen days. The purpose was to demonstrate the normal variability in the results of the two-hour uptake technique from day to day in the same individual and the range of variation among different subjects. It was found that the daily variability was remarkably small and the range among the 3 subjects very narrow. These results are shown in Table II.

Even with the total series of 75 control determinations in 48 patients (including the 30 studies shown in Table II), the wider range was not unexpected (12.9–21.5 per cent); the mean and standard deviation was quite reasonable (16.33 ± 1.74 per cent).

EFFECT OF CHOLECYSTOGRAPHY

Eighteen patients (9 male and 9 female) between twenty-seven and sixty-nine years of age were studied. On 12 of these patients, the last study was performed thirty days after oral cholecystography. In the remaining 6 patients, the study was concluded between fourteen and twenty-one days. The results are presented in Figure 1.

The following comments may be made: (a) the fall of the two-hour radioiodine uptake after oral cholecystography (6 tablets of telepaque) was prompt (within twenty-four hours) and marked; (b) the low level uptake (2–5 per cent) persisted for about ten days with tendency to recover very slowly; (c) the rate of recovery was increased in the next ten to fourteen days and then leveled off. Half recovery was achieved in two to three weeks and full recovery in thirty days or more.

TABLE II

RESULTS OF TWO-HOUR RADIOIODINE UPTAKE IN CONTROL PATIENTS

Patient	Age	Sex	Per Cent Uptake of 10 Studies in Fifteen Days		
			Range	Mean	Standard Deviation
C.F.	42	F	15.4–16.6	16.23 ± 0.38	
H.W.	31	M	15.0–16.7	15.87 ± 0.64	
N.L.	29	M	14.0–17.1	16.14 ± 0.70	
Average				16.08 ± 0.45	

EFFECT OF INTRAVENOUS PYELOGRAPHY AND ANGIOGRAPHY

Thirteen patients (10 male and 3 female) twenty-six to sixty-one years of age were studied for the effect of intravenous pyelography and 9 patients (6 male and 3 female), thirty-eight to sixty-one years of age, were studied for the effect of angiography upon the two-hour radioiodine uptake. As the opaque media used in these procedures were the same (urokon and hypaque), the results, as presented in Figures 2 and 3, are discussed together.

Again there was a very prompt and marked fall of the radioiodine uptake which persisted at low levels for about a week and gradually rose to a half recovery level in about fifteen days and full recovery level in three to five weeks.

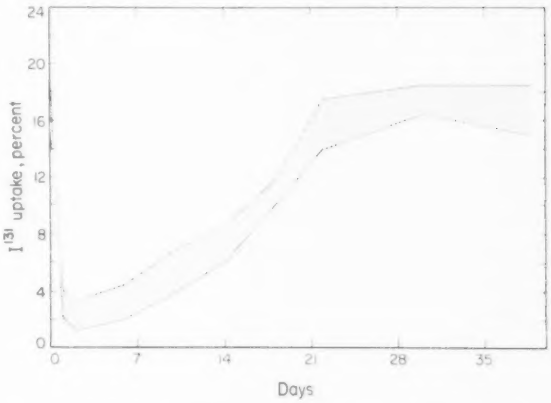

FIG. 2. Effect of intravenous pyelography upon thyroidal uptake of radioiodine. Plotted data represent mean ± standard deviation.

EFFECT OF BRONCHOGRAPHY

Five patients (3 male and 2 female), forty-seven to fifty-three years of age were studied for the effect of bronchography (dionosil, oily).

The results are similar to those in the preceding series. The half recovery time was about three weeks and full recovery time about five weeks (Fig. 4).

EFFECT OF MYELOGRAPHY

Twelve patients (6 male and 6 female), twenty-seven to sixty-four years of age were included in this study. In 2 patients, control radioiodine uptake before myelography and follow-up studies one, seven,

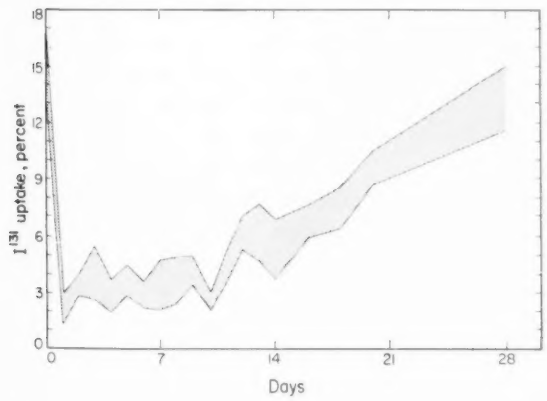

FIG. 1. Effect of cholecystography upon thyroidal uptake of radioiodine. Plotted data represent mean ± standard deviation.

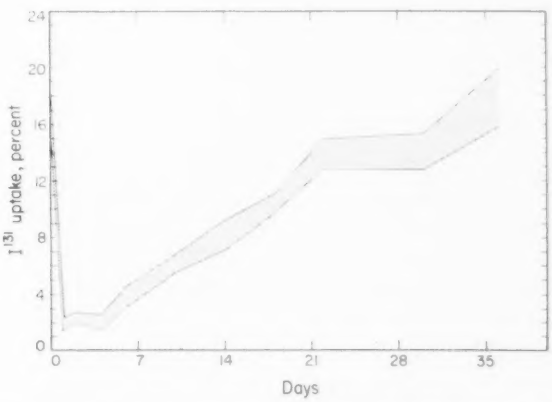

FIG. 3. Effect of angiography upon thyroidal uptake of radioiodine. Plotted data represent mean ± standard deviation.

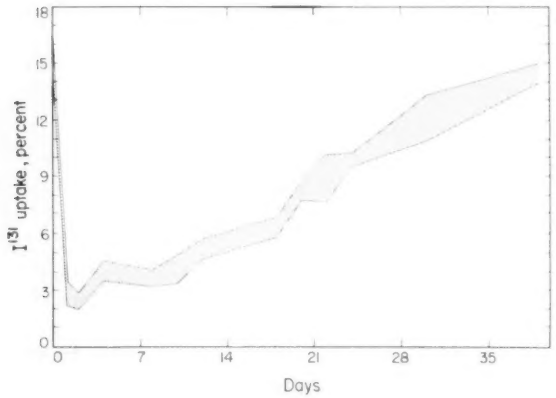

FIG. 4. Effect of bronchography upon thyroidal uptake of radioiodine. Plotted data represent mean ± standard deviation.

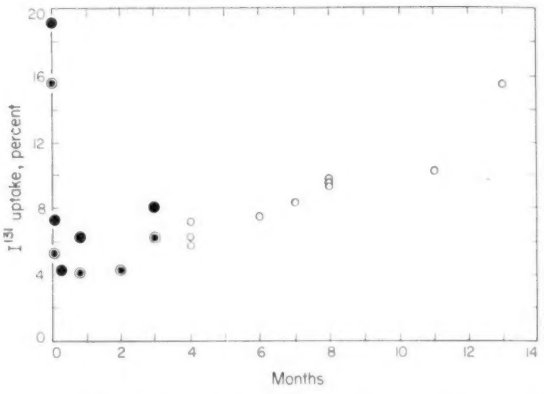

FIG. 5. Effect of myelography upon thyroidal uptake of radioiodine. The data from the serial studies of 2 patients are indicated by ● and ⊙. Each open circle represents a single study from a different patient at varying lengths of time following myelographic examination.

twenty-three days, two and three months after the contrast examination were carried out. Ten other patients were studied at varying lengths of time following myelographic examination.

In comparison with the results observed in the preceding series, it was noted that the reduction of thyroidal uptake of radioiodine was just as prompt but less marked, and the recovery took many months instead of weeks. These results are shown in Figure 5.

THE COMPARATIVE EFFECT OF VARIOUS IODINATED RADIOPAQUE MEDIA

For ease of comparison, the curves in Figure 6 are plotted with average values computed from the data of the several series presented above which are normalized against the average control values of each series taken as 100.

The following may be noted:

1. Patients having no thyroid dysfunction and having had no iodinated medication show very little day-to-day variation of the two-hour radioiodine uptake.

2. Iodinated radiopaque media commonly used in oral cholecystography, intravenous pyelography, angiography, bronchography and myelography interfere with thyroidal uptake of radioiodine tracer promptly, severely, and consistently.

3. The duration of the interference is markedly prolonged in the case of myelography (see Fig. 5).

4. Of the other opaque media, the degree of interference is equally severe; the duration is relatively short. There appears to be a quantitative difference, albeit slight, in the time of recovery among the several different media studied.

DISCUSSION

The interference with thyroidal uptake of tracer doses of radioiodine by inorganic

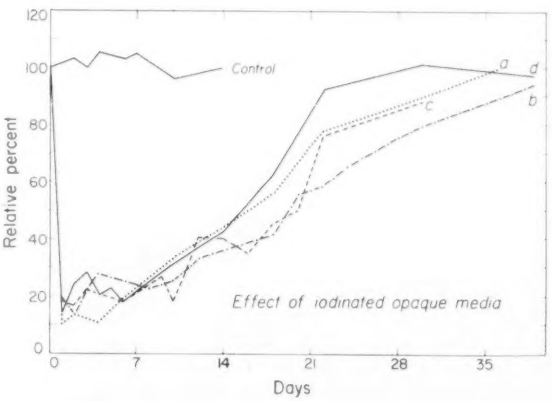

FIG. 6. Comparison of effect of iodinated opaque media upon thyroidal uptake of radioiodine. Curve *a* is for angiography; curve *b* for bronchography; curve *c* for cholecystography and curve *d* for intravenous pyelography. All data represented are average values of the series normalized against the average control values of each series taken as 100.

iodine was first recognized by Hamilton and Soley[4] and Hertz and co-workers[5,6] in their studies of both animals and humans. Similar effects of organic iodinated contrast media have been recorded by a number of authors.[1,2,3,8] Noteworthy among these is the study of Beierwaltes *et al.*[1,2] in which the blood protein-bound iodine and inorganic iodine were measured before and after the administration of Lugol's solution, telepaque, urokon and pantopaque. It was found that both of these values were promptly and markedly increased for seven to ten days immediately following the ingestion or injection of these substances. The rise of inorganic iodine was attributed to its pre-existence in the solution as well as to the process of deiodination of the organic compounds in the body.

At the normal concentration of 1–5 μg./100 cc. of serum, the amount of inorganic iodine in the extracellular fluid pool totals 140–700 μg. It is readily understandable that the size of this pool may be increased up to 100 fold by the addition of 14–70 mg. of inorganic iodine from the opaque media.

Wolff and Chaikoff[9,10,11] have shown that the biosynthesis of thyroxin ceased as the serum concentration of inorganic iodide exceeded 20–35 μg. per cent, while iodine trapping was unimpaired.

With the increase in the size of the inorganic iodide pool, the reduction of thyroidal uptake of a tracer dose of radioiodine is to be expected and may be attributed to two mechanisms: (1) the increased dilution of the tracer proportional to the increase in pool size; (2) the flooding or saturation of the thyroid tissue by the sudden abundance of iodide in the serum.

Our observations of marked reduction of the two-hour radioiodine uptake must be attributed to the increased dilution of the tracer as a major factor in the first seven to ten days, when the serum level of iodide is greatly increased as demonstrated in the studies of Beierwaltes.[1] It is important to realize that, although the uptake of radioiodine is reduced, the trapping of iodide is increased.[7,8]

With the serum iodide concentration returning to normal levels after the first seven to ten days following opaque media administration,[1] the dilution of the tracer dose ceases to be an important factor, and saturated storage of iodine during the days of bounty becomes the major cause of the persistent depression of radioiodine uptake,[10,11] which returns to normal in the course of three to five weeks as the iodine store in the thyroid gland is gradually reduced. In the case of myelography, droplets of pantopaque remaining in the subarachnoid space are a reservoir of iodine responsible for the indefinite depression of the radioiodine uptake.

CONCLUSION

The clinical implications of the observations made from a quantitative study of the effect of iodinated opaque media upon the radioiodine uptake by the thyroid gland may be stated as follows:

1. The results of radioiodine uptake studies must be interpreted with care.

2. Radioiodine uptake study should be done before roentgen diagnostic examinations requiring the use of iodinated radiopaque media.

3. A period of four to five weeks following the use of iodinated radiopaque media must be allowed before an accurate result may be obtained from radioiodine uptake studies, and a longer period following myelography.

Ching Tseng Teng, M.D.
Jefferson Davis Hospital
Houston 3, Texas

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A NOTE ABOUT IODINE-CONTAINING CONTRAST MEDIA AND THE INTERFERENCE OF TERIDAX FOR CHOLANGIOGRAMS IN EVALUATION OF THYROID FUNCTION BY MEASUREMENT OF SERUM IODINE*

By EVELYN B. MAN, PH.D.
NEW HAVEN, CONNECTICUT

IN THE choice of iodine-containing contrast media, efficacy of roentgenographic visualization of a system and maximum reduction of toxic side effects have received careful consideration. In recent years clinicians and analytical chemists have found that determination of the protein-bound or butanol-extractable iodine (PBI or BEI) of serum[1,5] furnishes one of the most useful methods for studying thyroid function. Persistence of iodine-containing contrast media in the circulating plasma usually excludes measurement of the PBI or BEI during an interval of weeks or months (a few years for lipiodol), depending upon the chemical structure and excretion of each specific iodine-containing medium. The role of the liver and of bile in conjugation, destruction and excretion of thyroid hormone might be better understood by combined roentgenologic tests and measurements of thyroxine-like compounds in the blood stream. Thus, information on iodine-containing contrast media concerns not only the radiologist but also all investigators in the field of metabolism.

In 1957 Astwood[1] reported PBI values of 6,600 and 4,500 μg. per 100 ml. of serum eight and nineteen months after gallbladder roentgenographic visualization with teridax (3-(3-hydroxy-2,4,6-triiodophenyl)-2-ethylpropionic acid). Figure 1, a reproduction from his article, shows PBI values of about 2,000 μg. per 100 ml. three years after teridax. From the semilogarithmic plot it was calculated that, for reduction of the spurious PBI to about 1 μg. per 100 ml. of serum, an individual must live thirty-three years after a single dose of teridax.[1]

The purpose of this note is to report that Astwood's data on elevations of serum PBIs seem also to pertain to increase of serum BEI values after teridax. An incomplete search of our records has revealed 13 BEI determinations on 11 patients whose serum iodine concentrations were above 50 and possibly above 1,000 μg. per 100 ml.[2,5] at intervals of three to forty-eight months after the ingestion of teridax. (In our method, the sensitivity of the ceric sulfate-arsenite measurement of iodide is qualitative rather than quantitative for concentrations above 50 μg. per 100 ml.)

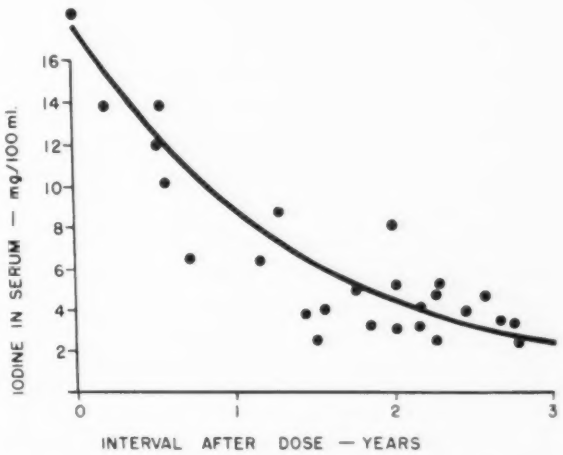

FIG. 1. "Concentrations of iodine in the sera of 15 patients at intervals after administration of teridax. The curve was derived by fitting a straight line to a semilogarithmic plot of the data." The iodine is expressed in mg., a unit 1,000 times the usual microgram unit for a serum PBI. (Reproduced with permission from The Transactions of the Association of American Physicians.[1])

* This project was supported in part by Research Grant A-392 from the United States Public Health Service.

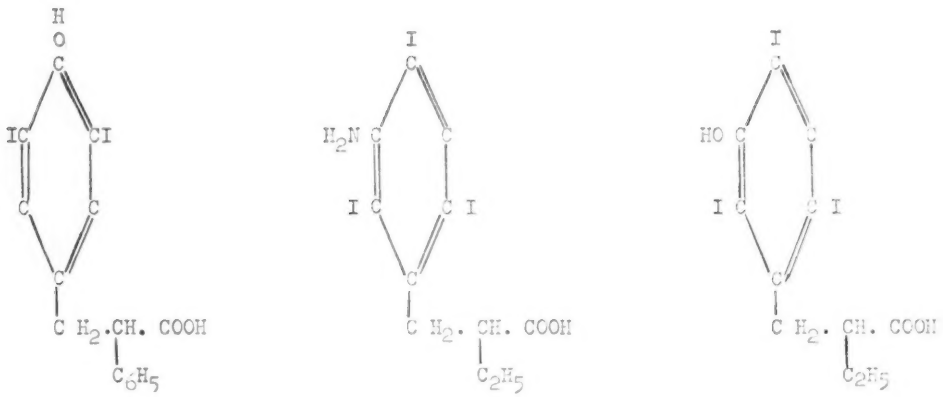

Fig. 2. Structural formulae.

The histories of these patients failed to reveal recent ingestion of inorganic or organic iodine compounds. In the diagnosis of thyroid dysfunction, introduction of excessive amounts of radiopaque iodine-containing contrast media into the laboratory via even a single serum destroys accuracy of other diagnostic PBI and BEI determinations. Laboratory glassware adsorbs the excess iodine; false high values are found for other sera analyzed simultaneously; contamination by a single sample is especially harmful in the time-saving techniques in which many serum samples are ashed in one muffle furnace.[4]

Of the contrast media which are used for cholangiography, telepaque or iopanoic acid (3-(3-amino-2,4,6-triiodophenyl)-2-ethylpropionic acid) is excreted quite rapidly (Fig. 2). Priodax (3-(4-hydroxy-3,5-diiodophenyl)-2-phenylpropionic acid) persists somewhat longer than telepaque. Some years ago serum protein-bound iodines were observed to return to normal for that individual by fourteen to sixteen weeks after the use of priodax.[6] Slingerland[10] noted mild increases of the PBI above 8 μg. per 100 ml. months after priodax. There was considerable variability between individuals. Rogers and Robbins[9] found that the PBI of one individual had returned to the control concentration one hundred and seven days after cholografin (N-methylglucamine salt of N,N′-adipyl-bis-(3-amino-2,4,6-triiodobenzoic acid)). Even two weeks after administration of a normal dose of telepaque, the BEI may be below 20 μg. per 100 ml.—a range often found in hyperthyroid individuals. By ten to twelve weeks after a single dose of telepaque given to patients without frank gallbladder disease, BEI values have returned to the normal range.

Structural formulae in Figure 2 demonstrate that telepaque differs from teridax only in substitution of an NH_2 group for an OH group. Iodine at the 2,4,6 positions around the benzene ring occurs not only in telepaque but also in hypaque and urokon. These contrast media have not been found to contaminate BEI values more than about twelve weeks although only one patient has been observed for each of these latter substances. Priodax, which may be excreted in sixteen weeks, has an OH group, but it is on carbon 4 and only two iodine atoms are on carbons 3 and 5 of the benzene ring. Thus the question arises whether the specific benzene group, with an OH on carbon 3 and 3 iodines at the 2,4,6 positions, produces a compound resistant to destruction or excretion by man.

Fecal excretion of teridax was not observed,[7] and relative absence of radiopaque material in the colon after teridax has been reported frequently.[3,7,11,14] In comparative clinical studies of teridax and telepaque in routine cholecystography,[11–14] only slight traces of opaque material were noted in the colon after teridax, but 97.4 per cent of the individuals had residual or excreted contrast medium in the colon after telepaque. Astwood isolated crystals of a compound similar to teridax from the blood stream and emphasized the abnormally long residence of this compound in the body.[1] He found that bound iodine of serum declined initially at a somewhat faster rate than during the subsequent slow phase of his logarithmic plot (Fig. 1). In dogs, during the phase of most rapid removal from the body, the iodine of teridax was reported to have been excreted in the urine,[8] but 14 per cent of the iodine of teridax was the maximum of the dose recovered even twenty-three days subsequent to oral administration. Removal of the gallbladder does not seem to alter persistence of the iodine-containing substance in the human blood stream; one of the elevated BEI levels found in our laboratory was forty-four months after cholecystectomy. Although toxicity from teridax was not revealed in animal experiments lasting twelve weeks unless dosage was excessive,[7] certain clinicians have inquired about unphysiologic consequences from persistence of such a foreign compound in the body. It seems important to investigate the excretion and destruction of any other contrast media containing the 3-hydroxy-2,4,6-triiodophenyl group of teridax (Fig. 2) before administration of such compounds to man.

CONCLUSION

One of the most useful methods for studying thyroid function is the determination of the protein-bound or butanol-extractable iodine of serum. Administration of the gallbladder medium, teridax, has been predicted to destroy the usefulness of this method for thirty-three years. Since other reliable media, such as telepaque, persist only about three months after visualization of the gallbladder, cautious cholecystographic use of teridax is urged.* This information about teridax is an example of the different effects of contrast media in basic medicine.

Department of Internal Medicine
Yale University School of Medicine
New Haven, Connecticut

We appreciate greatly Dr. E. B. Astwood's encouragement to publish more information on the residence of teridax in the blood stream and his gracious permission to reproduce Figure 1.

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* Since this manuscript was submitted for publication, serum BEIs of 2 newborns (of women who had received teridax more than two years before the birth of the infants) have been estimated to be about 4,000 μg. per 100 ml. of serum. From these data it is inferred that teridax crosses the placental barrier.

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IRRADIATION OF THE OVARIES FROM THE URINARY EXCRETION OF IODINE 131*

By F. COMAS, M.D., *and* M. BRUCER, M.D.
OAK RIDGE, TENNESSEE

WITH the widespread use of I^{131} in the treatment of several thyroid conditions, many investigators are concerned about the amount of radiation reaching the ovaries. It is feared that temporary or permanent sterility, miscarriages, or mutations in the offspring might occur later on.[1]

Although these dangers have been debated fairly often, mostly from a theoretic and philosophic point of view, as yet little information is available on the amount of radiation absorbed by the ovaries. This radiation is made up of three components: (a) beta and gamma radiation from the I^{131} present in the ovaries; (b) gamma radiation from the I^{131} localized in thyroid tissue; and (c) gamma radiation from the I^{131} excreted by the kidneys and accumulated for varying periods of time in the urinary bladder. (This will be referred to as "urinary ovarian dose.") The purpose of the study was to obtain numerical values for the urinary ovarian dose under the conditions prevailing in the clinical use of radioactive iodine.

To that effect an experimental model was set up to measure the dose rate to the ovaries as a function of bladder volume. The urinary ovarian dose was then calculated by applying the experimental results to data on urinary excretion of I^{131}.

METHOD

A female pelvis was simulated by using a 30 cm. by 25 cm. by 18 cm. lucite water phantom into which a bone pelvis was submerged. For "bladders" we used five glass containers, which held 50, 150, 280, 310, and 500 ml. The containers were filled with 80 to 100 mc of I^{131} and positioned one at a time in the center of the pelvis, so that the base was at the level of the lower border of the symphysis pubis. The recording instruments were two Victoreen 25 r chambers placed symmetrically on both sides of the pelvis, as shown in Figure 1. The ionization chambers were calibrated (with a flux of cobalt 60 gamma rays) against a sister chamber, which had been calibrated by the National Bureau of Standards.

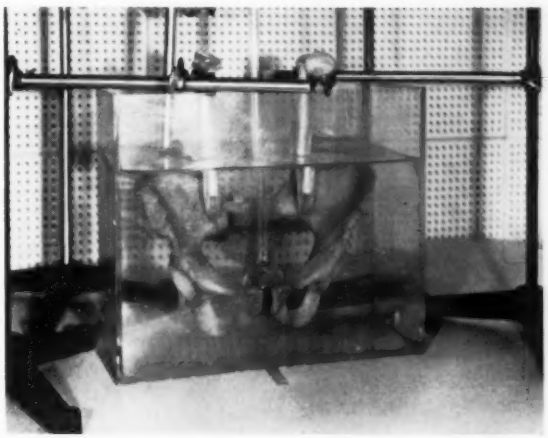

FIG. 1. Experimental setup showing lucite water-phantom with human bone pelvis submerged in it, and one of the artificial "bladders" and ionization chambers in place.

Readings were taken for each of the five full "bladders," and the recorded number of roentgens divided by the exposure time (from two to five hours) gave the dose rate corresponding to each bladder volume. The results were normalized for an I^{131} concentration of 1 μc per ml. and plotted in the first graph (Fig. 2), from which the dose rates in millirad per hour can be found for any bladder volume ranging from 50 to 500 ml. The readings were converted to rad without any correction factor. The small error introduced by this procedure will be quite insignificant in comparison with the uncertainty of the numerical values.

Although efforts were made to duplicate in our model the anatomic relationships

* From the Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tennessee, under contract with the United States Atomic Energy Commission.

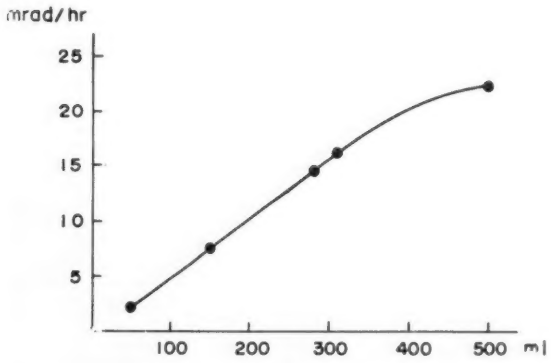

Fig. 2. Relationship of bladder volume to dose rate. The curve has been normalized for a concentration of 1 μc of I^{131} per 1 ml. of urine.

that occur in a female pelvis, it is realized that only a rather crude approximation was achieved. The "bladder" shape was globular, which is true for a distended bladder but not for one containing small amounts of urine. The base was placed at the level of the inferior border of the symphysis pubis; this is a compromise between the position in a young woman, which is a little higher, and that in a patient with mild cystocele so frequently present in older women. Greater difficulties were met in deciding where in the pelvis to lodge the "ovaries" (ionization chambers). In real life they occupy their standard anatomic position only in young women; mainly because of the pulling of the parametria as the uterus enlarges with each pregnancy, the ovaries later on wander off and in fact can be found anywhere in the pelvis. We made preliminary measurements in several positions and found the highest readings when the ionization chambers were placed at 1.5 cm. in front of the sacroiliac joint and 1.0 cm. below the brim of the pelvis, close to the lateral pelvic wall. Those were the figures used.

We were not able to position the ionization chambers so accurately that they would register exactly the same reading on both sides. The maximum difference encountered was 27 per cent. To diminish the error, we used the average of the two values. The decay of I^{131} during the time of exposure was not taken into account; it was about 2 per cent in five hours.

It is expected that the absorption and scattering of the I^{131} gamma rays in the model were nearly the same as those in the female human pelvis, because water behaves very much like soft tissue; a bone pelvis was used to simulate the real condition as closely as possible.

Application of the Experimental Results to Urinary I^{131} Excretion Data

The manner in which the experimental values (relationship of dose rate to bladder volume) are applied to calculate the urinary ovarian dose could best be understood by following the entry and discharge of urine into the bladder (urinary cycle). In the beginning the bladder is empty, it contains no I^{131} and therefore the ovaries are not irradiated. As urine flows from the kidneys to the bladder, the ovaries start receiving radiation at dose rates constantly increasing as the bladder expands. At a certain point the patient voids and the irradiation ceases momentarily, to start immediately with the next urinary cycle. A urinary cycle is defined as the time between two consecutive micturitions.

A plot of all the instantaneous dose rates during one urinary cycle would give us a curve, limiting an area that represents the urinary ovarian dose. To draw such a curve we have two values to start with. The initial dose rate is zero, because we assume that there never is any residual urine. The final dose rate, which is given in Figure 2 from our experimental model, corresponds to a bladder volume equal to the amount of urine voided. If we further assume that in one urinary cycle the I^{131} concentration and the flow of urine from kidneys to bladder are constant, the dose rate at any time can also be read in Figure 2. For instance, if one urinary cycle lasted nine hours and the volume of urine voided was 320 ml., at 4.5 hours the volume should have been 160 ml., which corresponds to a certain dose rate of Figure 2. In that way we can plot as many dose rates as we want. This was done in Figure 3 for an actual case. (When dose rates are plotted the values of Figure 2 are

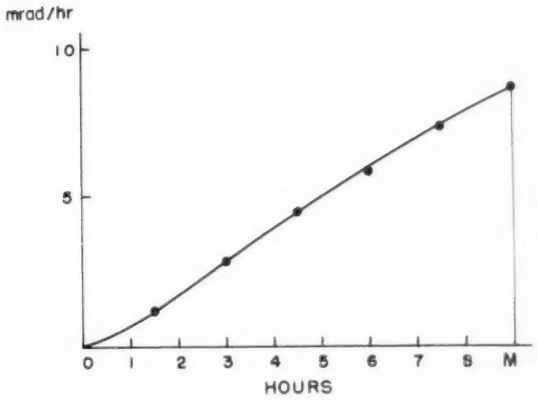

FIG. 3. The ordinates represent the instantaneous dose rates. The area under the curve is the amount of radiation absorbed by the ovaries from time 0, right after a micturition, to time M when the next micturition occurs.

always multiplied by the urinary concentration of I^{131} in μc per ml.)

The area under the curve can be measured by planography. To draw curves for each urinary cycle, and for all the patients, and to measure them would be a rather tedious undertaking. A short cut is possible, however, because Figure 2 shows an almost linear relationship between the dose rate and bladder volume up to large, rather unphysiologic bladder volumes. This being so, operations are much simplified by taking the dose rate corresponding to half the bladder volume (from Fig. 2) and multiplying it by the time of the urinary cycle. Then this dose rate must be multiplied by the urinary concentration of I^{131}, since Figure 2 was normalized for a concentration of 1 μc of I^{131} per ml. The result is given in mrad.

For instance, a patient voided 350 ml. of urine at 11:30 A.M. The last time she had urinated was at 2:30 A.M. (Time, nine hours.) The urine contained 19.3 mc of I^{131}. (Concentration, 61 μc per ml.) The dose rate to the ovaries for a bladder volume of 350 ml. is 15.5 mrad per hour (from Fig. 2).

Urinary ovarian dose from 2:30 A.M. to 11:30 A.M.:

$$9\times\frac{15.5}{2}\times 61 = 4{,}254 \text{ mrad}$$

The doses at the end of each micturition were added to obtain the total ovarian dose.

For our calculations we need to know the time interval between two consecutive micturitions, the volume of urine voided, and the amount of I^{131} in it. In the patients we studied, we had this detailed information for only the first 48 hours after administration of I^{131}. In the following days the 24-hour urine was collected in one single container and assayed. To do our calculations it is not possible to take the half volume of the entire daily urinary output and multiply it by 24, because this would reproduce a nonexisting situation, in which the bladder would be extremely distended at the end of the day. Instead we took an average bladder volume, which equals the volume of urine voided in one day divided by 6.8 (the average number of times the patients in our hospital voided in 24 hours). It is evident that with all those simplifications and "corrections" the results will be rather inaccurate. Actually, when we compared the results obtained by using the short method with the more laborious way of adding the urinary ovarian dose for each micturition, we found discrepancies ranging from -37 per cent to $+52$ per cent.

RESULTS

We had data on the urinary excretion of I^{131} in 7 patients; 2 of them were studied after a second dose of I^{131} had been given. Some pertinent clinical features are summarized in Table 1.

All the patients were in the hospital. Among the 4 hyperthyroid patients, one (No. 4 and 5) had a severe thyrotoxicosis and heart failure with anasarca, fast auricular fibrillation and other symptoms. The other 3 had milder degrees of hyperthyroidism. The 3 hypothyroid patients had had a total thyroidectomy as a first step toward radioiodine treatment for carcinoma of the thyroid. Patient No. 8 had metastases that showed slight I^{131} uptake. Patient No. 9 had no evidence of local tumor recurrence or metastasis. The patient represented by No. 6 and No. 7 had

TABLE I

CLINICAL FEATURES OF 7 PATIENTS WITH THYROID DISEASE, WHO HAD THEIR URINE ASSAYED FOR CONTENT OF I^{131}

No.	Age	Diagnosis	24 Hour Thyroid Uptake (per cent)	Clinical Degree of	
				Hyperthyroidism	Hypothyroidism
1	56	Graves's disease	67	++	
2	33	Graves's disease	48	+	
3	54	Nodular goiter	68	++	
4	64	Graves's disease	72	+++	
5	64	Graves's disease	72	+++	
6	64	Thyroid cancer	—		+
7	64	Thyroid cancer	—		+
8	51	Thyroid cancer	—		+
9	41	Thyroid cancer	—		+++

numerous pulmonary and osseous metastases, which showed considerable avidity for radioactive iodine. In all of them the urine was obtained separately for each micturition during the first 48 hours and the volume and I^{131} content were recorded. After the third day the 24-hour urine was measured up to a maximum of ten days.

Table II shows the total urinary ovarian dose in mrad during the time the experiment was carried out. The last column shows the urinary ovarian dose normalized to mrad/mc of I^{131} given to obtain better comparison among the patients.

A high percentage of the I^{131} urinary excretion takes place during the first 24 hours, and therefore the urinary ovarian dose is also relatively high during this time, as it can be observed in Table III.

It will be seen that only patients No. 8 and No. 9 eliminated all the I^{131} given during the time the experiment lasted. The others retained a considerable part of the radioisotope, which was slowly eliminated over many weeks. This late elimination will, however, add little to the total urinary ovarian dose because only small amounts of I^{131} are excreted every day and the isotope is decaying.

The average urinary ovarian dose for the hyperthyroid group was 24 mrad/mc,

TABLE II

TOTAL URINARY OVARIAN DOSE IN 4 HYPERTHYROID AND 3 HYPOTHYROID PATIENTS

No.	I^{131} Given (mc)	Days Urine Was Assayed	I^{131} Excreted (per cent)	Ovarian Dose	
				(mrad)	(mrad/mc)
1	5.2	7	20	62	12
2	6.5	7	52	201	31
3	5.1	10	45	163	32
4	5.1	10	19	73	14
5	5.2	6	37	140	28
6	1.0	10	45	29	29
7	100.5	10	48	2,753	27
8	102.0	4	99	9,984	98
9	1.0	2	100	141	141

TABLE III

URINARY OVARIAN DOSE ON THE FIRST AND SECOND DAY AFTER INGESTION OF I^{131} AND AT THE END OF THE EXPERIMENT. ALL FIGURES WERE NORMALIZED TO MILLIRAD PER MILLICURIE INGESTED

No.	Urinary Ovarian Dose in mrad		
	First Day	Second Day	Total
1	9	0.4	12
2	26	2.2	31
3	22	2.4	32
4	10	2.5	14
5	24	2.1	28
6	22	2.8	29
7	11	1.4	27
8	73	19.0	98
9	117	24.0	141
Average of hyperthyroid group			24

which is roughly five times smaller than that in the hypothyroid group. The patient indicated by No. 6 and No. 7, although showing symptoms of incipient myxedema, had an ovarian dose similar to that of the hyperthyroid group, probably on account of the I^{131} retained by the metastases.

DISCUSSION

Because the urinary ovarian dose cannot be measured *in vivo*, it has been necessary to make use of I^{131} excretion data and apply them then to an experimental model. It has been assumed that the conditions in our experiments were those actually prevailing in the human body. The assumptions involved have been:

1. The concentration of I^{131} in the urine does not vary during the time between two consecutive micturitions. This could be best clarified by taking urine samples at short intervals. Although this was not done with our patients, enough is known about the urinary excretion of I^{131} to test the validity of the assumption. The kidneys clear a fixed plasma volume of its iodide content at a constant rate, which Myant *et al.*[5] found to be 32 ± 12 ml. of plasma per minute in normal persons. McConahey and associates[3] reported similar figures for euthyroid and hyperthyroid patients and a clearance of 17.9 ± 1.6 ml. per minute for hypothyroid patients. In renal disease the values are naturally lowered. How much I^{131} is eliminated with the urine then depends on and parallels the plasma level of organic radioactive iodine. This varies rapidly during the first 24 to 48 hours after administration of I^{131} and in a different manner according to the functional status of the thyroid gland. Three minutes after ingestion, I^{131} is already found in the blood and in half an hour the highest plasma levels have already been reached in normal and hyperthyroid patients; in patients with hypothyroidism the peak occurs in about two hours. From then on the content of inorganic I^{131} in the plasma decreases rather rapidly; thus only a small and rather constant amount is present after about 24 hours in hyperthyroid patients, between 24 and 48 hours in euthyroid patients, and three to five days in hypothyroid patients. The protein-bound I^{131} has no bearing on our problem because the kidneys do not excrete it as such. It is apparent that our first assumption is a considerable simplification and that, especially during the first hours after administration of I^{131}, the urine concentration may be varying while the bladder is being filled. This fact will introduce a considerable error in the calculations; its magnitude will vary with the functional status of the thyroid, frequency of micturitions, and other factors.

2. The flow of urine from the kidneys into the bladder is constant in the time during two consecutive micturitions. It is well known that the rate of formation of urine varies widely according to muscular exertion, digestion, and fluid intake. It is believed, however, that there are no great differences in the relatively short time during which the bladder starts filling until it empties itself. Some persons may go many hours during the day without voiding, but this is an exception for which it is difficult to make corrections.

3. The assumptions involved in the calculation of the 24-hour urinary ovarian dose are obviously artificial ones; we hope that the errors they cause may compensate each other. Otherwise, during the first two days the calculations were based on the probably more accurate method of treating each micturition separately. After the third day there is not much inorganic iodine to be excreted, because what is left in the body is for the most part firmly bound to thyroid hormone.

It is evident that no great reliance can be placed in the figures given, which can probably vary as much as ± 100 per cent. They should, however, indicate the order of magnitude of the urinary ovarian dose.

COMMENTS

It should be interesting to determine how much the radiation from the I^{131} ez-

creted with the urine contributes to the total ovarian dose. This is due mostly to the beta irradiation from the I^{131}, which happens to be inside the ovary itself, and can be calculated by means of Marinelli and co-workers' formula.[4] This formula was slightly modified, as proposed by Loevinger *et al.*,[2] using the latest known values for the average energy of the I^{131} beta rays, and to obtain a result in rad. In addition, we assumed that the gamma contribution was 15 per cent of the beta dose.

Data on the concentration of I^{131} in the ovaries are scanty and can be obtained only from assays, autopsies, or surgical material. Table IV gives the ovarian doses calculated from 4 patients (other than those mentioned) and the values we were able to find in the literature.

Although the spread of values is considerable, the comparison of the averages from Table III and Table IV shows that the urinary ovarian dose is about 100 times smaller than the ovarian dose from the I^{131} inside the ovaries in hyperthyroid and euthyroid patients, and twenty times smaller in hypothyroid patients.

The gamma radiation reaching the ovaries from the I^{131} localized in the thyroid gland is insignificant. An approximate calculation shows that if 10 mc is in the thyroid gland, and taking the effective half life of I^{131} as six days, the radiation reaching the ovaries to complete decay is about 1.5 mrad.

TABLE IV

OVARIAN DOSE FROM THE I^{131} INSIDE THE OVARY, NORMALIZED FOR 1 MC OF I^{131} ADMINISTERED*

Case No.	Ovarian Dose in rad/mc
I	2.43
II	0.14
III	0.21
IV	3.85
(1)	6.6
Average	2.64

* Recalculated from Trunnell *et al.*[6] Average of 3 patients.

SUMMARY

The urinary ovarian dose (the amount of radiation absorbed by the ovaries from the I^{131} excreted by the urine and collected in the urinary bladder) has been calculated. To this end use has been made of I^{131} excretion data on 7 patients; these data have been applied to an experimental model. The urinary ovarian dose in our hyperthyroid patients averaged 24 mrad, and 98 and 141 mrad per mc of I^{131} ingested in the 2 hypothyroid patients. These values represent only about 1 and 5 per cent of the total amount of radiation absorbed by the ovaries of women receiving radioactive iodine.

F. Comas, M.D.
Oak Ridge Institute of Nuclear Studies
P. O. Box 117
Oak Ridge, Tennessee

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RADIATION EXPOSURE OF NONRADIOLOGIC HOSPITAL PERSONNEL DURING TREATMENT OF PATIENTS

By CARL E. NURNBERGER, Ph.D.*
MEMPHIS, TENNESSEE

SOME groups of people in hospitals may be exposed to radiations from radioactive substances although they do not work directly with these substances. The groups include nurses, aides and other ward personnel, relatives and friends of radioisotope patients,† and patients who are not being treated with radioisotopes. Individuals in the groups may never handle radioisotopes, but professional responsibilities, or relationship to patients, may bring them into the immediate vicinity of radioisotope patients and thereby result in radiation exposure. If common precautions of radiation protection are ignored, members of the groups will be exposed and the doses of radiation received can exceed permissible levels.

The purpose of this investigation was to examine the potential radiation exposure of the people mentioned above and, if indicated, to formulate safety rules for use in this hospital. The exposure of operating room personnel which occurs during administration of radioisotopes is not included in this investigation. The problem considered here is radiation exposure to personnel, visitors and nonradioisotope patients by radioisotope patients after radioisotopes are administered and the patients are returned to their rooms. Moreover, the primary concern is not the prevention of specific body injury, but maintenance of the average dose to the whole population to as low a level as reasonably possible.

Radiation safety practices pertaining to nurses, visitors and patients are often inconsistent with the degree of hazard involved.‡ Natural radioisotopes, chiefly radium and radon, are commonly used in hospitals without apparent concern for people who might be exposed. On the other hand, in the same institutions, induced radioisotopes are handled with extreme care and much attention is directed to the protection of everybody concerned. Actually, the radiation hazards associated with radium may exceed the hazard associated with induced radioisotopes.

In order to determine radiation exposure which might be received on entering the room of a radioisotope patient, surveys of a number of rooms were made. The patients in these rooms were undergoing treatment with one or the other of the following radioisotopes: radiogold (Au^{198}), radiocobalt (Co^{60}), and radium (Ra^{226}). In each case, the isotope was applied internally. Colloidal radiogold had been injected into the paracervical tissues of the pelvis, metallic cobalt cells were grouped in a vaginal cervical applicator, and radium needles were distributed in a uterine capsule and vaginal colpostat. Each was used for the treatment of cancer of the cervix uteri.

The patients were lying in bed when the surveys were made. Neither the patient nor the room was given special preparation for the surveys. The results, therefore, represent normally existing conditions.

Typical results are shown in Figure 1. The broken lines represent isodose rates which lie in a horizontal plane at the level

† The term "radioisotope patient" means any hospitalized patient who has had a radioisotope—natural or induced—administered internally, while "nonradioisotope patient" means any hospitalized patient who has been admitted for any purpose other than radiation treatment.

‡ The term "hazard," as used here, means a situation in which anybody might receive doses of radiation in excess of presently specified permissible levels. This does not mean that the exposed individual will suffer immediate consequences, but it does mean that his radiation tolerance has been lowered and that the probability of genetic effect has been raised.

* Radiological Physicist, Baptist Memorial Hospital.

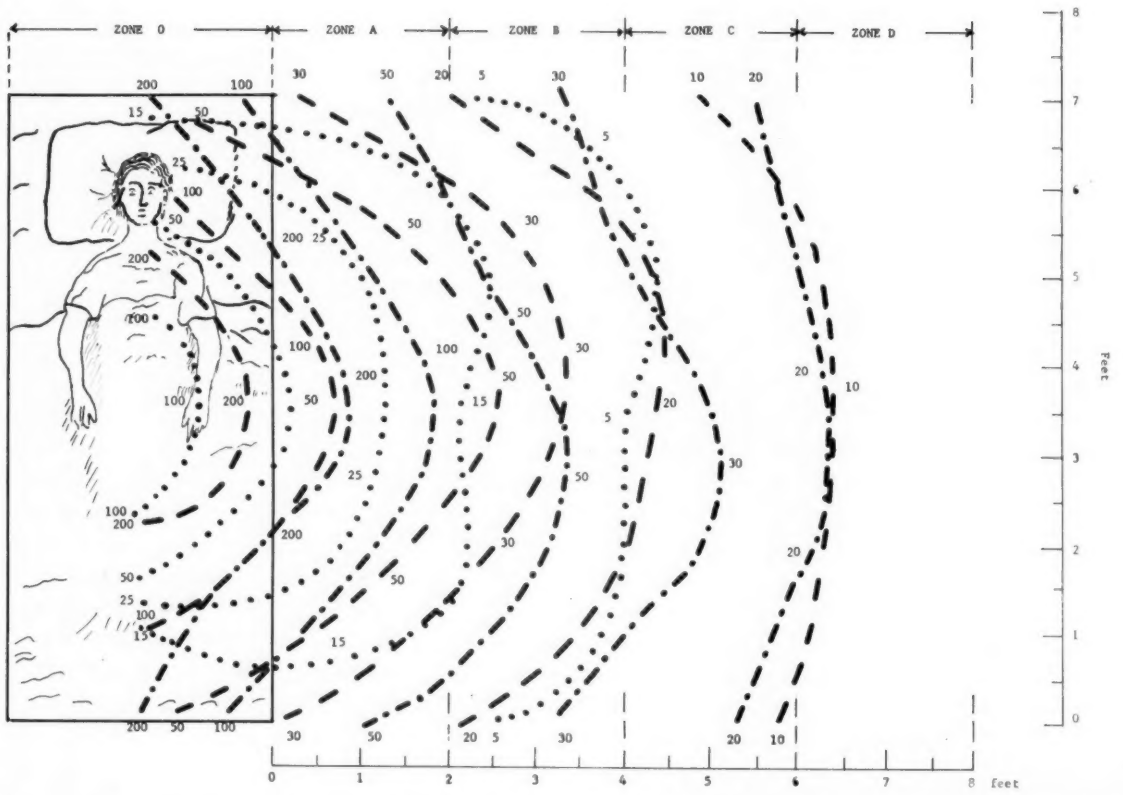

FIG. 1. Isodose rate curves around the bed of a patient during radioisotope therapy. Numbers represent milliroentgens per hour. ●—●— Co^{60} therapy, 100 mc; — — — Ra^{226} therapy, 100 mc; ●●●●● Au^{198} therapy, 100 mc.

of the patient's body; *i.e.*, about four feet above the floor. Dose rates are expressed in milliroentgens per hour (mr/hr.), and the rates listed in Figure 1 are rates at the beginning of treatment. As anticipated, the degree of radiation hazard in the patient's room increased in the following order: Au^{198}, Ra^{226}, and Co^{60} when identical activities of these substances were used. Moreover, dose rates from 25 to 200 mr per hour were recorded at approximately one foot from the patient's bed. A few hours of service at the bedside of these patients could result in significant exposure.

Precise determination of the radiation dose which is received by an individual who enters the patient's room and moves about at random cannot be had from the data in Figure 1. Likewise, specification of permissible occupancy of the room for this individual would be difficult. His exposure could be measured by means of film badges or pocket dosimeters, but the use of these devices under these circumstances is inadvisable. Our experience has demonstrated that many nurses and members of the public, too, become needlessly fearful, almost bordering on panic, when they are made to wear badges or pocket dosimeters. On the other hand, simple instructions on occupancy of the room are accepted and obeyed without emotional upset.

The space around the patient's bed was divided into zones. Zone O included the space occupied by the patient's bed and the space beyond the head and foot of the bed. Each of the other zones—Zones A, B, C, and D—were two feet wide. They were parallel to the length of the bed and their respective centers were 1, 3, 5 and 7 feet from the bedside. The average dose rates at the midpoints of the zones were determined. The results are given in Table 1.

Zone O, or the part of Zone O which is

TABLE I

RADIATION DOSE RATES AROUND A PATIENT UNDERGOING RADIOISOTOPE THERAPY

Zones		Milliroentgens per Hour*				
		First Day	Second Day	Third Day	Fourth Day	Fifth Day
A	Au^{198}†	27	19.6	15.7	11.8	8.0
	Ra^{226}	85	85	85	85	85
	Co^{60}	175	175	175	175	175
B	Au^{198}	7.8	6.3	4.9	3.8	2.8
	Ra^{226}	36	36	36	36	36
	Co^{60}	60	60	60	60	60
C	Au^{198}	2.8	2.0	1.6	1.2	1.0
	Ra^{226}	16	16	16	16	16
	Co^{60}	30	30	30	30	30
D	Au^{198}	0.9	0.7	0.5	0.4	0.3
	Ra^{226}	8	8	8	8	8
	Co^{60}	18	18	18	18	18

* Average values for each 24 hour interval at the center of the zones.

† Initial activity of the radioisotopes, each 100 mc. Dose rates increase or decrease proportionally to increase or decrease of activity.

inside the radioisotope patient's room, was not particularly hazardous. This is true because hospital rooms are usually small. There is no free space at the head of the bed and no "sitting" space at the foot. Consequently, the radioisotope patient is the only person who occupied that part of Zone O which is in the patient's room. But Zone O did not end in the patient's room. It extended into adjoining rooms also. The situation in an adjoining room can be hazardous. For example, 50 mc of Co^{60} in the pelvis of a patient would deliver about 100 mr per hour to the wall at the head of the bed. Attenuation of gamma rays by the wall and diminution of intensity by distance would still permit a patient in an adjoining room to receive as much as 25 mr per hour. If the treatment were two days long, the patient in the adjoining room would receive 1,200 mr. This dose exceeds the maximum permissible yearly accumulated dose for nonoccupational exposure.

Before permissible work hours for nurses and visiting hours for relatives and friends can be set up, the maximum permissible accumulated doses for these people will have to be decided. Decisions of this kind should comply as far as possible with the recommendations of the National Committee on Radiation Protection (NCRP).[1] The most recent recommendations, however, do not cover specifically the situations which pertain to some of these people. The decision on permissible dose must be based, therefore, on factors such as reason, judgment, and experience.

The people under discussion can be divided into two groups according to permissible accumulated doses (Table II). Nurses, aides, and ward personnel, as one group, are not classified as radiologic personnel, although the circumstances pertaining to their exposure are similar to those of the radiologic personnel. Radiation exposure of them is "occupational." They receive the exposure knowingly and willingly, but the frequency of exposure is not predictable. The safety factor for them, therefore, must be comparable to radiologic personnel, but with one exception. The maximum dose of 12 r in any one year as governed by the thirteen week limitation should not be allowed inasmuch as ade-

TABLE II

MAXIMUM PERMISSIBLE RADIATION DOSE TO NONRADIOISOTOPE HOSPITAL PERSONNEL

Groups	Type of Exposure	Maximum Permissible Dose* (Accumulated)	
		Yearly	Weekly
Nurses Aides Ward Personnel	Occupational	5,000 mr	230 mr†
Relatives‡ Friends Nonradioisotope Patients	Nonoccupational	500 mr	Not specified

* Total body irradiation.
† A dose of 230 mr per week is permissible only if the accumulated dose in any one year does not exceed 5,000 mr.
‡ It is assumed that members of these groups will not receive radiation exposure in the manner described in the text more often than once per year.

quate past and current exposure records of the group are probably nonexistent. A reasonable and permissible dose for nurses, aides, and ward personnel is considered to be 230 mr of total body exposure per week in any thirteen consecutive weeks, but the total accumulated dose per year should not exceed 5,000 mr.

The other group—relatives, friends, and patients not receiving radiation therapy—are exposed in semicontrolled areas under normal operations within the areas. They may or may not know that they are being exposed. Patients who are admitted to the hospital for reasons other than radiation therapy are most probably exposed without their consent. The exposure which the second group receives is "nonoccupational." The NCRP recommends a maximum permissible accumulated dose of 500 mr in any one year for this type of exposure. The probability of repeat exposures to the same individual is extremely low. A liberal estimate is one exposure per year. On this basis, a reasonable maximum permissible exposure per case—either as visitor or patient—is 500 mr of total body exposure.

Maximum permissible doses for the groups are summarized in Table II. Based on the data in Table II and on the zonal dose rates listed in Table I, maximum permissible occupancy times for the zones in the radioisotope patient's room were calculated and are compiled in Table III. Permissible occupancy times are listed for treatment periods from one to five days in length. Visits to the room, however, must be timed so as to divide the total exposure equally among the days of visit. The five day limit has no special significance, except that in most cases of internal administration of Co^{60} and Ra^{226}, the treatments are completed in five days or less. In most Au^{198} cases, the activity has decayed to a low level within five days, and the patients are permitted to leave the hospital.

The data in Table III are applicable to nurses, aides and ward personnel. To apply them to visitors and nonradioisotope patients, multiply the tabular values by 2.2. The data are not applicable to children. Children should not be permitted to enter the rooms of radioisotope patients.

Rooms directly above and below the radioisotope patient need not be restricted. On the basis of the above maximum permissible dose recommendations, these rooms may be occupied full time by the same individual.

From Tables I, II and III, it is quite evident that radiogold—the radioisotope which at present is used with the greatest attention to protection, including a radioactive precaution sign posted on the door of the patient's room, specifications of the earliest discharge data from the hospital,

Table III

MAXIMUM PERMISSIBLE OCCUPANCY TIMES IN ROOMS OF RADIOISOTOPE PATIENTS

Number of Days of Visit and Permissible Daily Exposure	Radio-sotopes†	Permissible Hours of Occupancy*																							
		First Day				Second Day				Third Day				Fourth Day				Fifth Day				Total Permissible Hours of Visits			
		Zone																							
		A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D	A	B	C	D
1 da. 230 mr	Au^{198}	9	24	24	24																	9	24	24	24
	Ra^{226}	3	6	14	24																	3	6	14	24
	Co^{60}	1.3	4	8	13																	1.3	4	8	13
2 da. 115 mr	Au^{198}	4	15	24	24	6	18	24	24													10	33	48	48
	Ra^{226}	1.5	3	7	14	1.5	3	7	14													3	6	14	28
	Co^{60}	0.7	2	4	7	0.6	2	4	6													1.3	4	8	13
3 da. 77 mr	Au^{198}	3	10	24	24	4	12	24	24	5	16	24	24									12	38	72	72
	Ra^{226}	1	2	5	10	1	2	5	9	1	2	4	9									3	6	14	28
	Co^{60}	0.5	1.4	2.7	5	0.4	1.3	2.7	4	0.4	1.3	2.6	4									1.3	4	8	13
4 da. 58 mr	Au^{198}	2	7	21	24	3	9	24	24	4	12	24	24	5	15	24	24					14	43	93	96
	Ra^{226}	0.8	1.5	4	7	0.8	1.5	4	7	0.7	1.5	3	7	0.7	1.5	3	7					3	6	14	28
	Co^{60}	0.4	1	2	4	0.3	1	2	3	0.3	1	2	3	0.3	1	2	3					1.3	4	8	13
5 da. 46 mr	Au^{198}	2	6	16	24	2.5	7	23	24	3	10	24	24	4	12	24	24	5	16	24	24	17	51	111	120
	Ra^{226}	0.6	1.2	3	6	0.6	1.2	3	5.5	0.6	1.2	3	5.5	0.6	1.2	2.5	5.5	0.6	1.2	2.5	5.5	3	6	14	28
	Co^{60}	0.3	0.8	1.6	2.6	0.3	0.8	1.6	2.6	0.3	0.8	1.6	2.6	0.2	0.8	1.6	2.6	0.2	0.8	1.6	2.6	1.3	4	8	13

* Tabular times are applicable to nurses, aides, and ward personnel. For relatives, friends, and nonradioisotope patients multiply tabular times by 2.2. Based on division of the total radiation exposure equally between treatment days. Applicable to adults only.

† Tabular times are for 100 mc of each radioisotope. For greater or lesser activities multiply tabular times by the ratio: 100/mc used.

and limitations on visits to the radioisotope patient's room—is the least hazardous of the three radioisotopes surveyed. Special attention is called to this fact not for the purpose or intention of relaxing radiogold precautions, but in order to emphasize the need for more attention to protection when radium and radiocobalt are used.

SUMMARY

Recommendations on radiation protection for nurses, aides and ward personnel, for relatives and friends who visit radioisotope patients, and for nonradioisotope patients are summarized as follows:

1. Children and young adults under eighteen years of age should not be permitted to visit nor to be hospitalized in rooms occupied by radioisotope patients.

2. Hospital rooms immediately above and below radioisotope patients need not be restricted with reference to occupancy.

3. Radioisotope patients may be hospitalized with reference to other patients as follows:

a. Radiogold patients. They may be put in rooms with other patients provided that no parts of their beds are closer than four feet.

b. Radium patients. They may be put in rooms with other patients provided that no more than 50 mg. of radium is used and the beds are at least six feet apart.

c. Radiocobalt patients. They may be put in rooms with other patients provided that no more than 23 mc of Co^{60} is used and the beds are at least six feet apart. Internal administration of Co^{60} usually involves activities higher than 23 mc, therefore, these patients should be hospitalized in private rooms. The preferred room is one with an outside wall. The bed should be against the outside wall. Beds in adjoining rooms should be moved as far as possible from the Co^{60} patient's bed.

4. Nurses, aides and ward personnel may enter the rooms of radioisotope patients each day of the treatment period. Since the services which these people give to the patient are performed in Zone A, maximum permissible occupancy of the room is with reference to Zone A.

a. Radiogold patients. Nurses, aides, and ward personnel may attend radiogold patients for a total of 9, 10, 12, 14, and 17 hours, depending upon the number of days (from 1 to 5 days) of duty with the radiogold patient. For example, a nurse who will attend the patient three days is permitted a total of 12 hours at the bedside (Zone A).

b. Radium patients. Nurses, aides and ward personnel may attend radium patients at the bedside for a total of 3 hours regardless of number of days of treatment.

c. Radiocobalt patients. Nurses, aides and ward personnel may attend a radiocobalt patient at the bedside for a total of 1.3 hours regardless of number of days of treatment. If essential nursing services require more than 1.3 hours, then room care of radiocobalt patients should be divided between several persons in order that permissible levels of exposure are not exceeded.

5. Visitors may enter the rooms of radioisotope patients each day of the treatment period. The lengths of time and place where they should remain in the rooms are as follows:

a. Radiogold patients. Visitors may spend full time (24 hr./day) in the room of a radiogold patient provided that they remain in Zone C, or farther away from the bed.

b. Radium patients. Visitors may spend a total of 30 hours in the room of radium patients provided that they remain in Zone C, or farther away from the bed.

c. Radiocobalt patients. Visitors may spend a total of 18 hours in the room of radiocobalt patients provided that

they stay in Zone C, or farther away from the bed.

The above general recommendations are based on an activity of 100 mc of either radioisotope, except as noted otherwise. Dose rates are directly proportioned to activity, and occupancy times are inversely proportioned to activity. Thus, the permissible times specified in the previous paragraphs should be raised or lowered according to whether the activity used is less or more than 100 mc and according to the particular zone occupied.

Department of Radiology
Baptist Memorial Hospital
899 Madison Avenue
Memphis 3, Tennessee

REFERENCE

1. Maximum permissible radiation exposure to man. Addendum to National Bureau of Standards Handbook 59. April 15, 1958.

FOCUSED GRID TELECOBALT FILM DOSIMETRY*

By WALTER MAUDERLI, D.Sc.,† DAVID M. GOULD, M.D.,‡ *and* JOHN W. LANE, M.D.§
LITTLE ROCK, ARKANSAS

SUCH promising results were obtained by the use of grid telecobalt therapy on patients with advanced cancer that it was felt necessary to learn more concerning the dose distribution of the particular grid first used. The study of this grid led to the construction and investigation of other grids as a general problem in grid dosimetry. Questions arose such as what is the effect of hole diameter and distance between hole centers on the dose distribution? To answer these questions, we constructed twelve different grids. Three hole diameters and four different ratios of lead area to hole area ($L:h$) were selected. The hole diameters are 1/4 inch, 5/16 inch, and 3/8 inch. The ratios ($L:h$) for each hole diameter are 1:1.5, 1:2, 1:2.5, and 1:3 on the source side (Table 1). The ratio of $L:h$ (rather than the distance between the hole centers) is used here because this parameter is commonly used in conventional grid therapy at lower radiation energies. This ratio, however, is of less significance in this study, since the grid is 14.4 cm. from the skin surface. Because of the distance, the $L:h$ ratio does not follow the ratio of highly irradiated skin surface to relatively protected skin surface. This skin surface ratio is felt to be of more biologic significance.

The grid-skin distance measures 14.4 cm. because the grid was attached to the collimator. At this distance it is still possible to obtain good registration of the grid pattern for successive treatments by the attachment of a thin perforated metal sheet which lies on the skin surface. The only previous reference in the literature to grid telecobalt therapy described a grid which was placed flush upon the skin.[1]

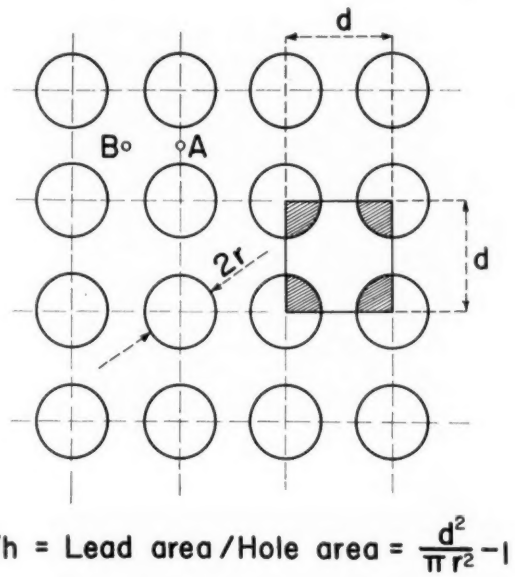

FIG. 1. Grid surface. The square indicates one grid cycle. A point midway between two holes is indicated by point A. Point B indicates a point equidistant from the centers of four holes.

CONSTRUCTION OF THE GRIDS

Holes were drilled in two sheets of asbestos. On one sheet, the distance between the hole centers was d, on the other, d' (Fig. 1 and 2). These two sheets were attached to an iron frame and cylindrical iron rods pushed through the corresponding holes in each sheet. The die was then heated and filled with molten lead. Because of the relatively large diameter of the cobalt 60 source, a conical shape for the holes in the lead grid was not felt to be necessary. Figure 1 does not show that the holes on the surface of the grid tend to become slightly more elliptical the farther they are from the center of the grid. All the grids are 56 mm. thick, which is about 5 half value

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† Assistant Professor of Radiation Physics.
‡ Professor of Radiology and Head of Department of Radiology.
§ Assistant Professor of Radiology.

TABLE I

	Grid-1		Grid-2		Grid-3		Grid-4		Grid-5		Grid-6		Grid-7		Grid-8		Grid-9		Grid-10		Grid-11		Grid-12		Row
Hole diameter	6.35 mm.		7.94 mm.		9.53 mm.		6.35 mm.		7.94 mm.		9.53 mm.		6.35 mm.		7.94 mm.		9.53 mm.		6.35 mm.		7.94 mm.		9.53 mm.		1
d, Source side d', Patient side	8.9 mm. 10.5 mm.		11.1 mm. 13.1 mm.		13.3 mm. 15.8 mm.		9.8 mm. 11.5 mm.		12.2 mm. 14.4 mm.		14.6 mm. 17.3 mm.		10.5 mm. 12.5 mm.		13.2 mm. 15.8 mm.		15.8 mm. 18.7 mm.		11.2 mm. 13.3 mm.		14.1 mm. 16.6 mm.		16.9 mm. 20.0 mm.		2
Area ratio: $L:h$ Source side Patient side	1.5 2.5		1.5 2.5		1.5 2.5		2.0 3.2		2.0 3.2		2.0 3.2		2.5 3.9		2.5 3.9		2.5 3.9		3.0 4.6		3.0 4.6		3.0 4.6		3
Field size for 50 per cent intensity at 50 cm. from source	15 mm.		12 mm.		14 mm.		11 mm.		12 mm		13 mm.		10 mm.		11 mm.		13 mm.		10 mm.		11 mm.		13 mm.		4
D, 50 cm. from source	15 mm.		18 mm.		22 mm.		16 mm.		20 mm.		24 mm.		17 mm.		21 mm.		26 mm.		18 mm.		23 mm.		28 mm.		5
Area ratio $L':h'$	0.3		1.9		2.1		1.7		2.5		3.3		2.7		3.6		4.1		3.1		4.6		4.9		6
Dose in hole center in percentage of dose in open field	59.5		71.6		80.3		58.7		72.3		85.3		59.3		71.7		83.4		56.9		73.4		82.1		7
Depth in cm.	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	
0.4	47.4	25.1	29.9	14.2	26.8	14.5	35.6	17.8	22.2	13.1	14.5	9.2	25.2	14.2	17.7	11.2	12.2	8.3	22.9	14.7	13.3	9.0	9.3	7.1	
3.5	64.2	36.0	37.0	18.9	33.9	19.9	43.7	23.7	29.9	17.8	18.7	13.1	34.0	19.7	22.0	14.2	15.1	10.9	26.4	18.5	16.0	12.7	12.8	10.9	
6.9	71.7	45.4	47.8	26.6	38.5	23.4	55.7	29.8	38.1	25.2	24.6	16.7	45.1	25.7	27.0	19.3	18.2	14.4	37.6	25.6	21.2	17.0	15.0	12.4	
10.7	79.9	53.1	55.2	31.6	45.0	27.9	68.4	39.4	48.6	32.9	30.4	21.5	57.8	33.2	33.2	23.6	21.6	17.0	47.0	30.7	27.5	21.7	18.6	17.1	
15.2	91.7	66.7	67.9	42.1	55.2	35.3	79.1	50.3	58.6	41.4	38.5	27.9	69.5	46.5	44.8	31.6	29.0	21.5	60.9	38.9	37.1	29.4	23.7	20.7	8
19.0	94.2	74.8	76.1	50.1	59.0	40.1	87.8	60.7	65.2	47.4	44.0	32.2	80.8	54.0	54.4	38.2	35.9	27.0	72.6	51.3	46.0	35.8	29.4	26.3	

Row 1. Grid hole diameter.
Row 2. Distance between hole centers on the side of the cobalt 60 source and on the patient side, respectively.
Row 3. Ratio of lead area to hole area on the cobalt 60 side and on the patient side, respectively.
Row 4. Approximate diameter of the field with 50 per cent or more of the hole center intensity (this field is not an exact circle).
Row 5. Distance between maximum intensities on the skin surface.
Row 6. Ratio of skin area with less than 50 per cent of the maximum intensity to that of more than 50 per cent of the maximum intensity.
Row 7. Maximum dose on the skin surface in percentage of open field dose.
Row 8. Percentage intensities at different depths in the phantom of projected points A and B (Fig. 7) The maximum intensity at every depth is assumed to be 100 per cent.

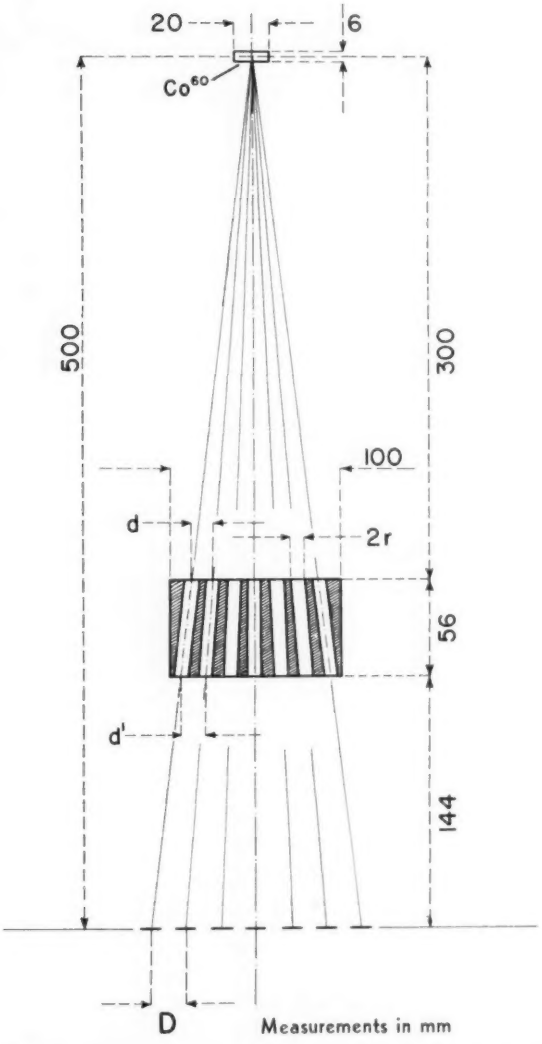

FIG. 2. Geometric arrangement of grids in relation to source and phantom surface.

layers for cobalt 60 radiation. The parameters of the 12 grids are listed in Table 1, rows 1, 2 and 3.

MEASUREMENTS

Films were exposed at different depths of a masonite phantom, using no phantom in back of the films.[2] The exposure time was selected so that the resulting maximum density was between 2 and 3. Calibration films were exposed and developed along with each series of films. The processing was carried out in an automatic Pako machine. The reproducibility was checked with ten films exposed under exactly the same conditions. Fluctuations have never been larger than ± 2 per cent at a density of about 2.5. For each depth, the dose was computed for points on the axis through a hole center and for points midway between 2 and 4 holes (Fig. 1, points A and B). Table 1, row 7 shows the relative dose at 4 mm. depth in the hole center compared with the open field dose. Figure 3 shows this relative dose as a function of hole diameter. The principal reason for the intensity drop as the hole size decreases is the fact that part of the cobalt 60 source becomes shielded by lead at smaller hole diameters. At the phantom surface, the cobalt 60 source becomes partly shielded for hole diameters less than 8 mm. At a depth of 20 cm. in the phantom, the source becomes shielded at hole diameters of less than 16 mm. Table 1, row 8 shows, for various depths, the ratio of the intensity between 2 and 4 holes (points A and B), respectively, to the intensity in the hole center. These data are an indication of the effectiveness of the grid in various depths. Figure 4 shows the depth dose curves for

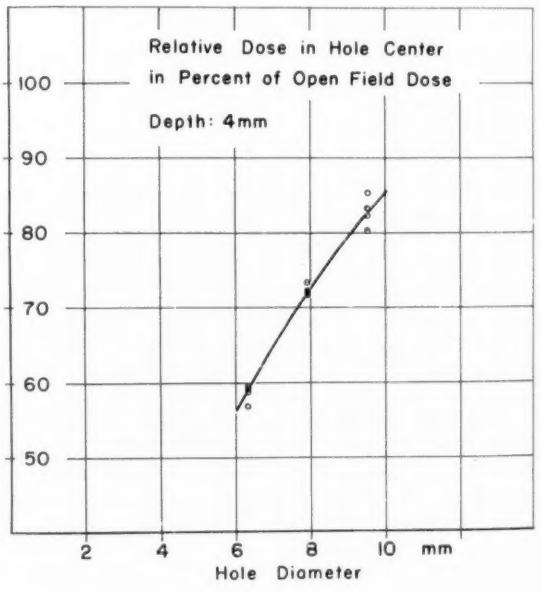

FIG. 3. Relative dose in hole center.

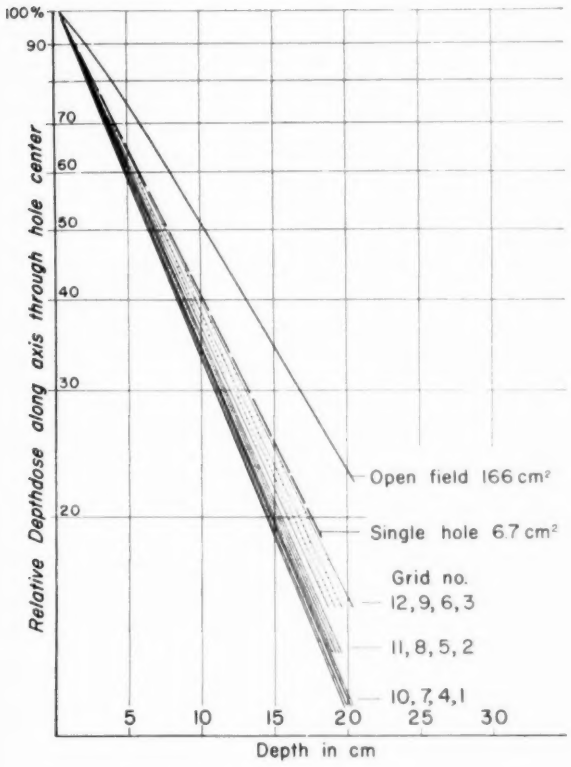

FIG. 4. Depth dose curves for points on an axis through the hole center.

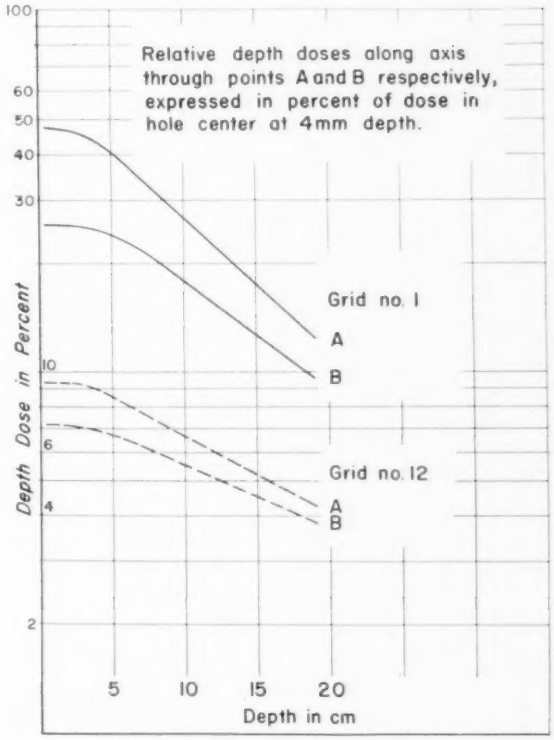

FIG. 5. Relative depth doses along axis through points A and B respectively.

different grids along the axis through the hole center; Figure 5 shows the depth doses for grids no. 1 and no. 12 along the axis through the points A and B (between 2 and 4 holes). For measuring the intensity distribution across the hole, a system was built to guide the films across the opening of the densitometer automatically. The measuring system is shown in Figure 6. The field measured by the densitometer is 1 mm. in diameter. The electrical circuit of the densitometer was so adjusted that the output was not proportional to the photographic density, but to the exposure in roentgens. Figures 7 and 8 give examples of the two extremes obtained with grids no. 1 and no. 12 of a scan across the hole centers. It is apparent that, for a depth of more than 11 cm., the effect of grid no. 1 becomes minute. One definition of the grid effect, f, from the standpoint of dosimetry can be based on the ratio of the maximum intensity at the hole center to the mean of the intensity at points A and B beneath the lead as follows:

$$f=\frac{2I_z}{I_a+I_b}-1$$

where I_z = intensity in hole center; I_a = intensity at point A; and I_b = intensity at

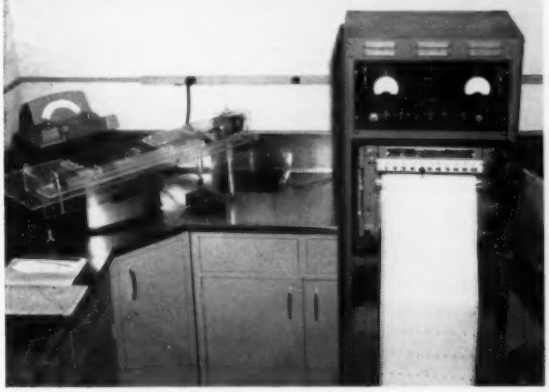

FIG. 6. Densitometer with attached automatic scanning device and chart recorder.

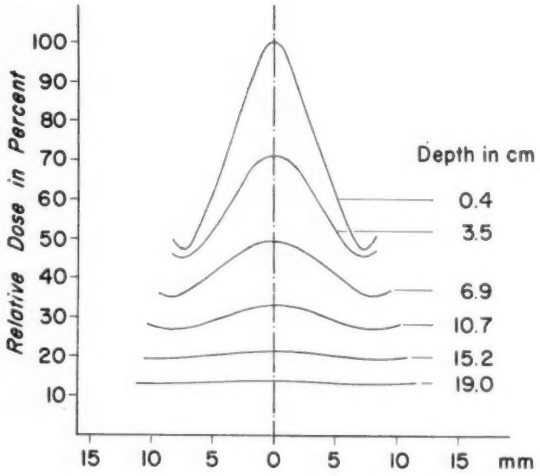

FIG. 7. Grid No. 1. Dose distribution across hole (along row).

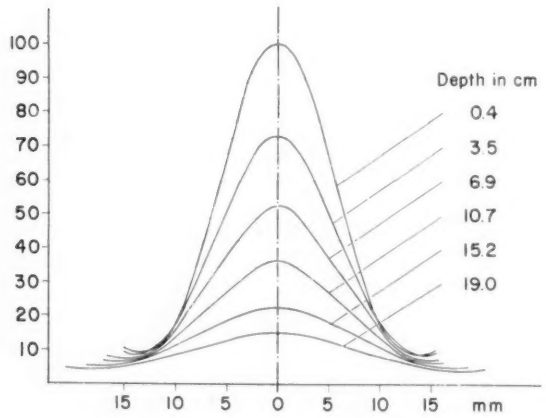

FIG. 8. Grid No. 12. Dose distribution across hole (along row).

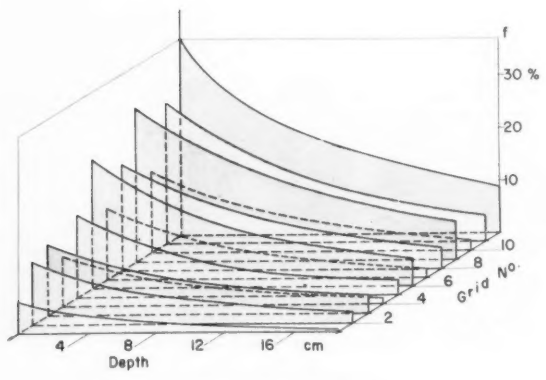

FIG. 9. Grid effectiveness, f, as a function of phantom depth.

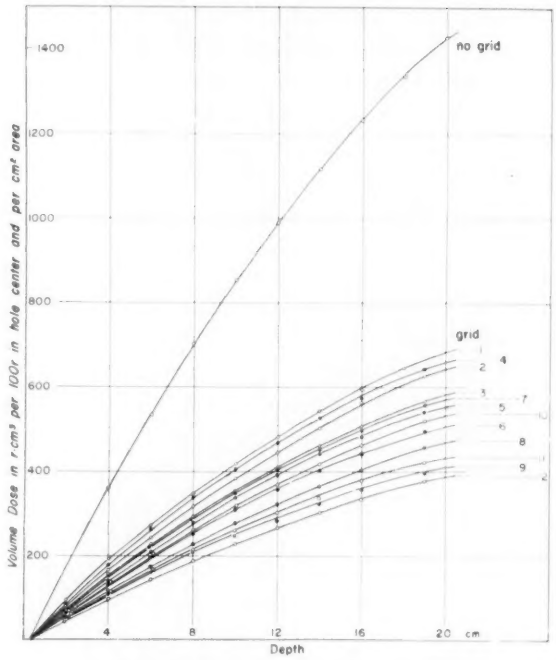

FIG. 10. Volume dose in roentgen·cm.^{3} for 100 r in the hole center at 4 mm. depth and per cm.^{2} of the skin area.

point B. For a homogeneous intensity distribution, f becomes 0. The maximum theoretic value for our particular grid thickness of 5 half value layers would be 30 (I_a and I_b=0.031 each, I_z=1). Figure 9 shows f in percentage of this theoretic maximum value.

COMPUTATION OF VOLUME DOSES

Because of the large diameter of the cobalt 60 source, a calculation of the volume doses is practically impossible. We have, therefore, computed the volume doses by film dosimetry. Each film was scanned over an area, the length of which was two hole cycles and the width one hole cycle. Each area was divided into eleven rows and each row scanned separately. For each grid, the dose in the center of a hole at a depth of 4 mm. was assumed to be 100 per cent. Each of the eleven curves was integrated with a planimeter. The resultant linear dose can be expressed in roentgen·cm. These doses were plotted on a graph. A new integration of this curve gave an area

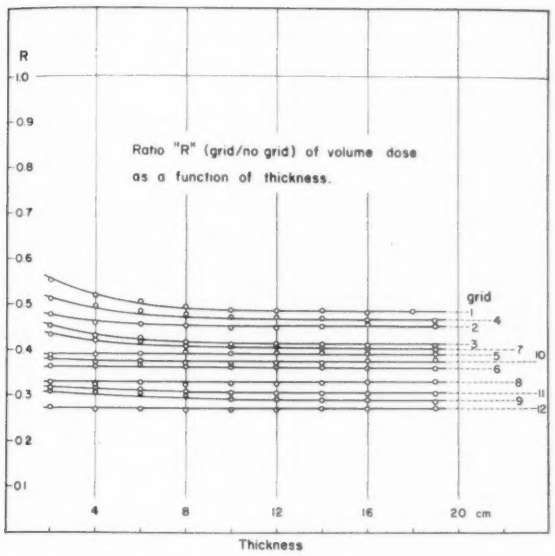

Fig. 11. Ratio of volume dose of the grid to the open field for the same skin areas.

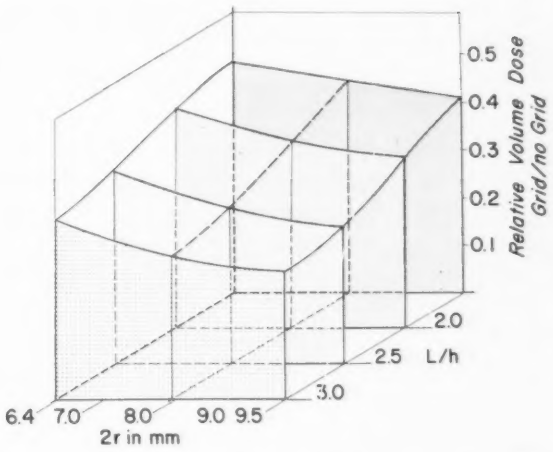

Fig. 12. Ratio of volume dose of the grid to the open field (for equal field sizes) as a function of hole diameter and the ratio $L:h$.

dose which may be expressed in roentgen·cm.^{2}. These area doses for the different depths of one particular grid were again graphed. Integration of these curves gave the volume doses, expressed in roentgen·cm.^{3}. The results for the twelve grids are shown in Figure 10, which gives the mean volume doses for 100 r in the hole center at 4 mm. depth and per cm.^{2} of the phantom surface. In calculating volume doses for practical purposes, the value is correct only when the area of interest contains at least one grid cycle. Figure 11 indicates the ratio of the volume doses of the grid to those of the open field. It is rather surprising that this ratio is independent of the thickness, when the latter is greater than 8 cm. Figure 12 gives the volume doses as a function of hole diameter and the ratio, lead to hole area, source side ($L:h$).

All measurements were carried out in the center portion of the field. For outside holes, an intensity drop of from 6 to 10 per cent was observed.

SUMMARY

Twelve grids, with varying hole diameters and hole separation, were studied relative to their effects upon cobalt 60 radiation fields. Each grid was constructed of lead with a thickness of 5 half value layers. By means of film dosimetry, depth dose curves and volume (integral) doses were determined and are presented for each grid.

Walter Mauderli, D.Sc.
University of Arkansas
Medical Center
Department of Radiology
Little Rock, Arkansas

The authors wish to thank Mr. Don Thompson for his technical assistance.

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FILM DOSIMETRY OF COBALT 60 RADIATION*

By WALTER MAUDERLI, D.Sc.,† DAVID M. GOULD, M.D.,‡ *and* JOHN W. LANE, M.D.§
LITTLE ROCK, ARKANSAS

DOSIMETRY of roentgen or gamma rays is carried out with ionization chambers whenever possible or practical because the most frequently used unit of radiation dose, the roentgen, is based on the ionization effect in air. Although it would be more desirable to measure absorbed radiation energy directly, it is either virtually impossible or so complex that it can not be used in everyday dosimetry.

Besides the ionization chamber, other detectors such as scintillation crystals or photographic films are used. Generally, the radiation response of these other detectors results in readings which must be corrected, depending upon the radiation energy. This correction is made in such a manner that the results will be proportional to the ionization measurements.

Some reasons for using other detectors rather than ionization chambers are the following: (1) In a high gradient of radiation intensity, the location of the effective measuring point becomes too vague even with the smallest available ionization chamber. (2) The size of a roentgen- or gamma-ray beam may be of the same order or even smaller than the dimensions of the ionization chamber. (3) The number of points to be measured may be so great that ionization measurements would be time-consuming. (4) The accurate placement of the ionization chamber may become too exacting and critical for practical use.

The problem of dosimetry in grid therapy is a practical example of how film dosimetry can overcome the obstacles imposed by the use of an ionization chamber. If the grids contain holes with diameters of from $\frac{1}{4}$ to $\frac{3}{8}$ inches, the use of a Victoreen thimble chamber is impossible. Measuring the intensity distribution across the hole or the rapid fall-off of intensity at the side of the field is out of the question with one of our small ionization chambers of 6 × 6 mm. One possible method would be the use of very small scintillation crystals. However, to determine the exact position of the crystal would be tedious, especially when measuring in the depth of a phanton. Furthermore, innumerable single measurements would be necessary if automatic scanning were not available.

For these reasons, measurements with photographic film would seem to be ideal. Films are very thin and the resolution in a lateral direction to the beam is of the same order as the size of the silver grain. In one single exposure, the amount of information gained is more than one can obtain by myriad measurements with either an ionization chamber or a crystal. Subsequent measurements of density at any number of points on the film can be quickly and conveniently made. On the other hand, the film has a serious disadvantage. Its response is due to the action of radiation on silver bromide molecules. Both silver and bromine have a relatively high atomic number compared to the elements in air. Therefore, the film response shows considerable wave length dependence in contrast to the ionization chamber.[1]

CALIBRATION: DENSITY VERSUS FILM EXPOSURE

Experimental Conditions. Radiation source: Cobalt 60 teletherapy unit (approximately 900 rhm). Ionization chamber: Victoreen condenser r-meter No. 1412, 25 r chamber. Film: Kodak Industrial Film Type M (unless otherwise indicated). Density measurements: Macbeth-Ansco

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† Assistant Professor of Radiation Physics.
‡ Professor of Radiology, and Head of the Department of Radiology.
§ Assistant Professor of Radiology.

Densitometer Model 12A. Phantom: Masonite 10×10 inches, specific weight = 1.08 g./cc. Distance: Source—phantom top (SPD) = 50 cm.

For calibration purposes, the film was placed between two layers of masonite, each 3 mm. thick. Figure 1 shows the relationship between density and exposure time in arbitrary units. Since the measurements are relative, the exposure unit is unimportant so long as it is proportional to ionization measurements.

The points in Figure 1 were obtained with films from four different shipments of Kodak Industrial Film Type M. Although the density, as a function of the exposure time, resulted in four different curves, it was possible to bring these curves to coincidence by a linear transformation of the time axis.

The linearized curve (dotted line) was accomplished by proper adjustment of the electronic circuit of the densitometer. In order not to disturb the calibration of the instrument, we have constructed an external adapter. The readings on the instrument were no longer a measure of density as defined, but were directly proportional to the dose or exposure of the film. The direct linear conversion from film response to exposure becomes especially important when films are automatically scanned and the data transcribed on a chart recorder.

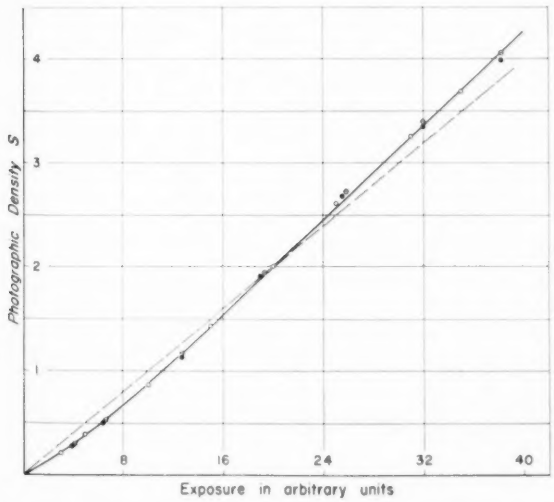

Fig. 1. Photographic density as a function of exposure time for Kodak Industrial Film Type M is indicated by the solid line. The dotted line shows electronically linearized response of the densitometer.

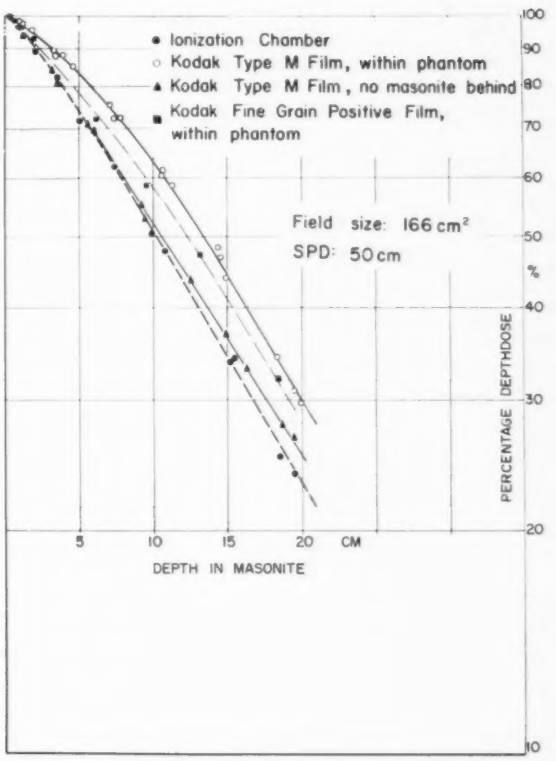

Fig. 2. Depth dose curves in masonite with the ionization chamber and film. Field size 166 cm.²; SPD (source-phantom distance) 50 cm.

COMPARISON OF IONIZATION CHAMBER AND FILM RESPONSE

Depth dose curves were measured with the ionization chamber for field sizes of 6.7 cm.², 64 cm.² and 166 cm.². In the smallest field, the proper position of the ionization chamber was controlled by radiography. Figures 2, 3 and 4 show the resulting depth dose curves.

Films were also exposed under the same conditions within the phantom. The exposure times (25 to 120 seconds) for the different depths were selected so that the resultant maximum density was between 2 and 3. Figures 2, 3, and 4 show the depth dose curves obtained with film. The rela-

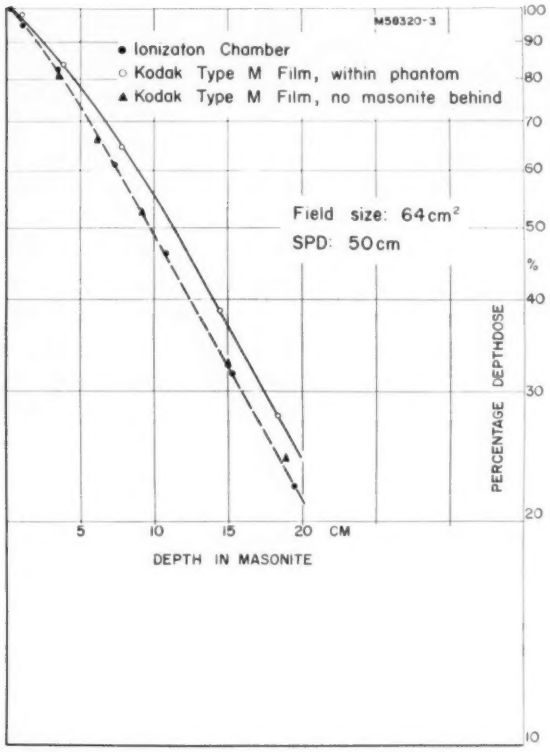

FIG. 3. Depth dose curves in masonite with the ionization chamber and film. Field size 64 cm.²; SPD (source-phantom distance) 50 cm.

tive exposure (computed from the calibration curve) in 4 mm. depth of the phantom is assumed to be 100 per cent.

Whereas ionization chamber and film doses correlate very well for the smallest field, there is an increasing deviation with increasing field size. For 166 cm.², and for a depth between 10 and 20 cm., the dose indicated by the film is about 1.3 times higher than that obtained with the ionization chamber. The same measurements with the Kodak Fine Grain Positive Film show a depth dose increase of about 1.2 times.

The properties of the photographic emulsion, especially the thickness, have an effect on the results. The total weight per unit area of the Kodak Industrial Type M Film is 29 mg./cm.² of which 7.1 mg./cm.² is due to the double emulsion. The thickness of the Fine Grain Positive Film is 20 mg./cm.² of which 1.6 mg./cm.² is the emulsion. A decrease in the thickness of an emulsion decreases the difference in the relative response between film and ionization chamber.

When the films are exposed under the same conditions, except that the portion of the phantom which backs the film is removed, the depth dose curves coincide with the ionization depth dose curves for all but the largest field. Even with the largest field, the difference at 15 cm. is only 6 per cent.

The lead grids studied have a maximum hole area less than 1 cm.². Although there are a great number of holes, the "effective" field size is much below the 166 cm.² for which there is still relatively good agreement between the ionization chamber and the film.

Figure 5 shows the "dose" computed from film exposures as a function of the thickness of the phantom backing the film.

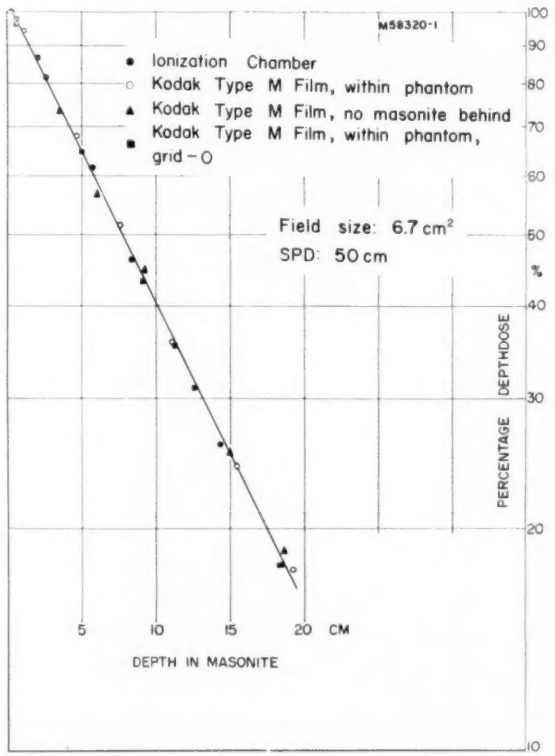

FIG. 4. Depth dose curves in masonite with the ionization chamber and film. Field size 6.7 cm.²; SPD (source-phantom distance) 50 cm.

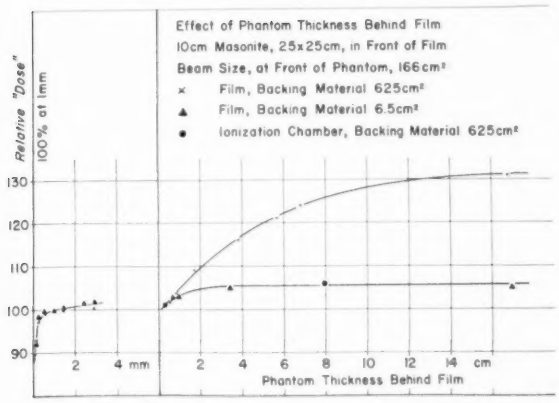

Fig. 5. Effect of phantom thickness behind film.

Paper was used below 0.5 mm.; between 0.5 and 10 mm. lucite and over 10 mm. masonite were the backing materials. Ten centimeters of masonite were placed in front of the film. The "dose" with 1 mm. backing material was arbitrarily chosen as 100 per cent. The "dose" shows a sharp increase between 0 and 0.25 mm. backing, and it is independent of the area of the backing sheets. This increase is caused by scattered electrons with energies of about 100 kev. With more than a few millimeters backing, the increase is slow and is due to Compton photon backscatter.

The difference between minimum and maximum backing is only about 5 per cent for an ionization chamber. The film, however, shows a 40 per cent difference. When only 2 mm. of masonite instead of 10 cm. is placed in front of the detectors, the difference in dose for maximum and minimum backing measured by the ionization chamber is 3 per cent and by the film 21 per cent.

The energy for Compton backscatter radiation (with a scattering angle of $\pi/2$ to π) for cobalt 60 is in the range of 209 to 269 kev. In the range of these radiation energies, most emulsions show an increased sensitivity compared to the primary photon energy of 1.25 mev. For multiple scattered photons with still lower energies, the sensitivity increase can be very large. These experiments show that the increase in the film sensitivity from backscatter is approximately seven to eight times that of the ionization chamber.

FORM OF DEPTH DOSE CURVE

The depth dose curve may be approximated by:

$$I = I_0 e^{-\mu x'} \left(\frac{D'}{D'+x'} \right)^2$$

where I = intensity at depth x', I_0 = intensity at depth 4 mm.,* D' = source-phantom distance + 4 mm., and x' = depth in phantom − 4 mm.

In a narrow beam, μ is nearly identical to the absorption coefficient for primary photons. In a broad beam, however, the apparent value of μ changes and is a function of the phantom depth x' and the field size. The slope of the logarithmic depth dose curve may be approximated by the formula:

$$\frac{d}{dx'}\left(ln \frac{I}{I_0} \right) = -\left(\mu + \frac{2}{D'} \right) - x' \left(\frac{d\mu}{dx'} - \frac{2}{D'^2} + \frac{2x'}{D'^3} - \frac{2x'^2}{D'^4} + \cdots \right)$$

for $x' \leq D'$.

For D' greater than 50 cm. and x' smaller than 15 cm., the slope change is mainly due to the term $\frac{2}{D'}$. The term containing x' results in a change of 8 per cent between 0 and 15 cm. phantom depth (assuming $d\mu/dx' = 0$). Except for very small fields, $d\mu/dx'$ can not be neglected and compensates more or less for the change in slope due to the square law. The nearly linear depth dose curves for smaller fields are, therefore, understandable.

RELATION BETWEEN AIR AND PHANTOM MEASUREMENT WITH IONIZATION CHAMBER

A few words about the precise depth of the ionization chamber in the phantom is not amiss. Figure 6 shows a typical ar-

* Average depth at which I reaches the maximum.

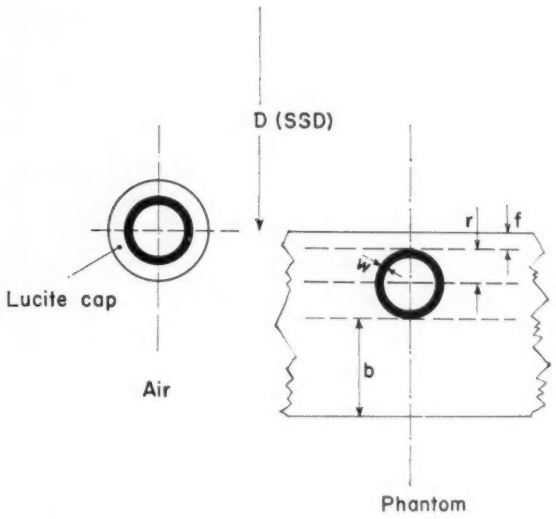

Fig. 6. Arrangement of ionization chamber for air and phantom measurements.

rangement. Frequently, the depth is considered $r+f=x$ (the distance between phantom surface and the center of the ionization chamber). Others consider the depth is $f=x$ (the distance between the phantom surface and the ionization chamber top). The real depth, x, is that depth at which the same result would be obtained with an infinitely small ionization or extrapolation chamber. x is between $f+w$ and $f+r$. For the 25 r Victoreen thimble chamber, r is 6 mm. and $w\sim 1$ mm. When reference was made to the phantom depth, x, we assumed $x=f+2$ mm. (for $f\geq 0$). The same assumption was made for the backing thickness, which is considered to be $b+2$ mm. The uncertainty in measuring x is assumed to be about 2 mm.

Tests were made to show the relationship of measurements in a phantom and in air. In air, the chamber was covered with a 4 mm. lucite cap. In phantom measurements, x was 4 mm. In both cases, the distance between the cobalt 60 source and the center of the chamber was 50 cm. The phantom reading was 4.5 per cent higher than the air reading for a 166 cm.^{2} field and 2 per cent higher for a 64 cm.^{2} field. No difference was found for a 6.7 cm.^{2} field.

When measurements in a phantom were made using the source to phantom top distance, the following results were obtained: The 4 mm. depth measurement was 1.5 per cent higher for the 166 cm.^{2} field than for the air measurement, 1 per cent less for the 64 cm.^{2} field, and 3 per cent less for the 6.7 cm.^{2} field.

SUMMARY

When, for purposes of dosimetry, films are placed within a phantom, backscatter effects were shown to be a source of considerable error even with high energy cobalt 60 radiation. This source of error can be eliminated by removing that portion of the phantom which is behind or back of the film. Under these conditions, the response of the film and the ionization chamber correlate well. Forward scatter does not disturb the correlation except to introduce a small error in large fields.

Walter Mauderli, D.Sc.
University of Arkansas
Medical Center
Department of Radiology
Little Rock, Arkansas

The authors wish to thank Mr. Don Thompson for his technical assistance.

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COBALT 60 RADIOGRAPHY*

By C. RICHARD PERRYMAN, M.D., D.Sc. (MED.), JOHN D. McALLISTER, M.D., *and* JAMES A. BURWELL, M.D.†
PITTSBURGH, PENNSYLVANIA

COBALT 60 teletherapy in recent years has assumed considerable importance in the practice of radiation therapy. Its merits as a treatment medium are being documented, but its diagnostic potentialities have not been explored to any significant degree despite the fact that Tuddenham and his associates[3] in 1953 stressed the potential value of radiographs produced by megavoltage equipment. Cobalt 60 radiography has been used in our therapy department since 1955.

The quality of radiographs made with high energy sources differs greatly from those made with conventional roentgenographic units, primarily because of the decreased differential absorption between bone and soft tissue. At lower energies, the attenuation of the roentgen-ray beam is almost entirely due to photoelectric absorption which is strongly dependent upon the atomic number of the absorbing material. The effective atomic number of bone is considerably higher than that of air, water and muscle, and it is thus easy to understand why osseous structures are better visualized than underlying soft tissues in conventional roentgenographic studies. However, as the energy of the beam of radiation increases, Compton scatter and absorption occur, and this is dependent upon the electron density of the absorbing material rather than its atomic number. Because of this, bone detail is not prominent on radiographs obtained by using megavoltage equipment.

When one considers that osseous structures can very often obscure underlying soft tissue lesions, the advantage of eliminating these structures becomes apparent. In cobalt 60 radiography, the obscuring osseous densities are reduced to a minimum and underlying soft tissue shadows are better visualized.

The radiographs accompanying this paper have all been produced by a Picker cobalt 60 teletherapy unit equipped with a Johns' collimator. We feel that good collimation eliminates much of the troublesome penumbra. Some of the films were exposed by a source of 1,000 curies of cobalt 60 and the others by a source of 2,800 curies. The focal spot of the cobalt 60 source is large, measuring 2.0 cm. in diameter in our early studies and 2.5 cm. in diameter in the more recent ones. Its large size has been a less important factor than was anticipated.

TECHNIQUE

The technique of cobalt 60 radiography is relatively simple. We use ordinary cassettes from which the usual intensifying screens have been removed and replaced by lead intensifying screens 0.01 inch in thickness. The lead screens reduce the number of very low energy secondary electrons reaching the film and also provide a dense layer of material near the film, increasing the probability of a Compton collision with production of higher energy electrons which lose that energy on the film.

Industrial type film has been used and three types have been employed: Eastman Kodak type AA, Ansco type Superay B and DuPont type 506. We have experimented with all three types in an attempt to improve the quality of our work.

In taking an ordinary diagnostic posteroanterior 14×17 inch radiograph of the chest, we use a source skin distance of 150 cm. and shutter openings of 20×20 cm. The best quality film usually requires a dose of approximately 2.0 r (Table 1). A lateral

* From the Department of Radiology, Mercy Hospital, Pittsburgh, Pennsylvania.
Presented at the Sixtieth Annual Meeting of the American Roentgen Ray Society, Cincinnati, Ohio, September 22–25, 1959.
† Fellow of American Cancer Society.

TABLE I

TECHNIQUE CHART FOR COBALT 60 RADIOGRAPHY

Region Radiographed	Film Size (in.)	Shutter Openings (cm.)	Exposure (r)	Source Skin Distance (cm.)
I. Diagnostic Studies				
a. Head and Neck (lateral)	10×12	20×20	1.8	100
b. Chest (posteroanterior)	14×17	20×20	2.0	150
c. Stomach (anteroposterior)	14×17	20×20	2.2	100
II. Port Film Localization				
a. Treatment Port for Head, Neck or Chest				
(1) First exposure	10×12 or 14×17	Treatment field size	1.4	80
(2) Second exposure		20×20	1.4–2.0	150
b. Treatment Port for Uterus or Bladder (lateral)				
(1) First exposure	14×17	Treatment field size	2.4	100
(2) Second exposure		20×20	4.7	120

diagnostic radiograph of the nasopharynx requires a source skin distance of 100 cm. and shutter openings of 20×20 cm. with an exposure of 1.8 r. A diagnostic radiograph of the stomach is taken immediately after the patient has ingested a glass of carbonated beverage. The patient is positioned according to the location of the lesion. If the lesion is in the fundus or proximal portion of the stomach, the exposure is made in the erect position (Fig. 12). An exposure of 2.2 r is made at a source skin distance of 100 cm. with shutter openings of 20×20 cm.

Most of our work has been concerned with the radiographic localization of lesions for the proper placement of the treatment port, and we should like to stress the importance of routine use of this simple technique which will so often increase accuracy of localization and thus prevent treatment failure. In this procedure, two exposures are made on the same film. The first exposure is made at our treatment distance of 80 cm. The shutters are open just enough to outline the field size we intend to use. A dose of approximately 1.4 r is then delivered to the film. This is the minimum exposure which the timer on our equipment permits. The second exposure is made at 100–150 cm. with the shutters open wide enough to include the whole anatomic area. This second exposure requires a dose of approximately 1.4 r to 2.0 r. The patient must not be allowed to move between the two exposures. When the second exposure is made, the increase in source skin distance creates a slight distortion of the field size which amounts to no more than 3 to 6 per cent.

When treating carcinomas of the bladder or uterus by rotational therapy, we localize the treatment port as follows: In bladder cases, a Foley catheter is inserted, the Foley bag filled with mercury, and the bladder partially filled with air. A lateral treatment port exposure is then made at 100 cm. source skin distance with 2.4 r. The second exposure is made at 120 cm. source skin distance and a 20×20 cm. shutter opening with 4.7 r (Fig. 4). In uterine cases, the radiographic technique is the same, using a metallic ring placed in the vagina adjacent to the cervix for anatomic localization.

All films are processed in rapid developer at 68° F. The 14×17 inch films are developed for eight minutes and the 10×12 inch films for six minutes. After a one min-

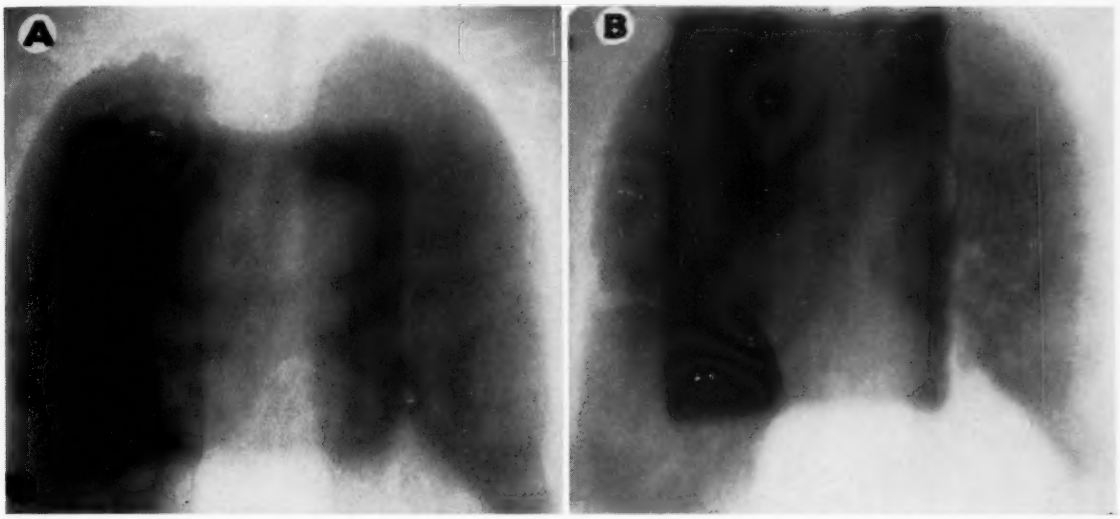

Fig. 1. (*A*) Cobalt 60 radiograph showing inadequacy of topographic localization of treatment port in carcinoma of lung. Tumor at superior margin of port would not be included in the treated area. (*B*) Cobalt 60 radiograph showing an adequate port for this lesion. Note the extrinsic pressure produced on the right side of the trachea by a tumor mass.

ute rinse, films are fixed for twenty minutes, then washed and dried in the usual manner.

We have not found that the thickness or region of the body to be examined appreciably influences the dosage required to obtain these radiographs unless the thickness of the part is more than 40 per cent greater than the average.

ILLUSTRATION OF CASES

The radiographs which are presented show the value of cobalt 60 or megavoltage radiography in demonstrating soft tissue lesions unsuspected on conventional roentgenograms. They also demonstrate the necessity of obtaining routine port radiographs of the treatment area to correct errors of topographic localization of tumors.

In viewing these radiographs, one will note that they confirm the fact that air is the best contrast agent in mega- or supervoltage ranges.

The selection of a treatment port for carcinoma of the lung is frequently difficult when one depends on topographic methods. Figure 1*A* shows such a treatment port which is obviously inadequate in size to cover the whole lesion. The superior limits of the tumor are not included in the treatment field. Figure 1*B* shows the corrected port for this extensive lesion and incidentally demonstrates marked extrinsic pressure on the right side of the trachea.

Tangential ports are commonly employed to treat recurrences of breast carcinoma on the anterior chest wall. It is extremely important, however, that the proper angle of the beam is used. Figure 2*A* shows a medial tangential field with the beam angled 20 degrees from the horizontal. This includes the skin, but only a minimal amount of lung tissue is irradiated. In Figure 2*B*, the angle of the beam was 35 degrees and, while the skin was included in the field, a great deal of normal underlying lung tissue was needlessly irradiated. We do not believe that the internal mammary lymph node chain is adequately included in this type of treatment port and, therefore, see no reason to irradiate more lung tissue than is necessary.

Port radiographs are taken of all areas being treated even though topographic localization would seem to be accurate in many instances. In Figure 3, a port for carcinoma of the esophagus is demonstrated. The radiograph incidentally shows a marked tumor infiltration into the left

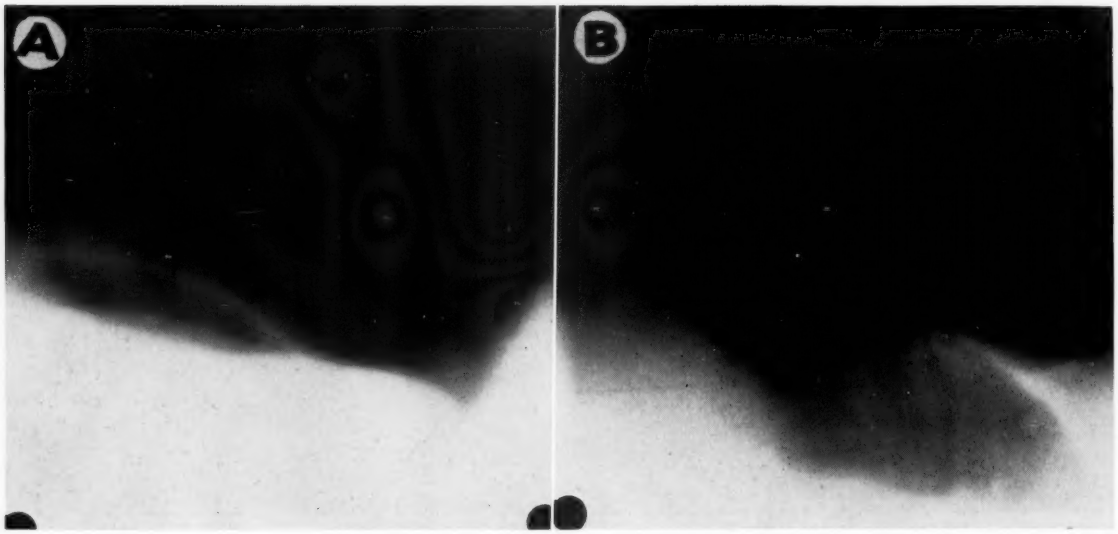

FIG. 2. (*A*) Tangential port used to treat skin recurrences in breast carcinoma. Note that only a small portion of lung tissue is included in the field. (*B*) Tangential port indicating that the angle of the beam should be changed because too much lung tissue would unnecessarily be irradiated.

main stem bronchus, which was not apparent clinically or on routine roentgenograms of the chest and esophagus.

Cobalt 60 radiographs are used extensively to localize lesions that are to be treated by rotational therapy. Figure 4 shows a localization radiograph for treatment of a carcinoma of the bladder. The previously described technique has been used, passing a Foley catheter into the bladder and filling the Foley bag with mercury. On the radiograph the mercury is well seen and also localizes the trigone of the bladder. The internal bladder wall is

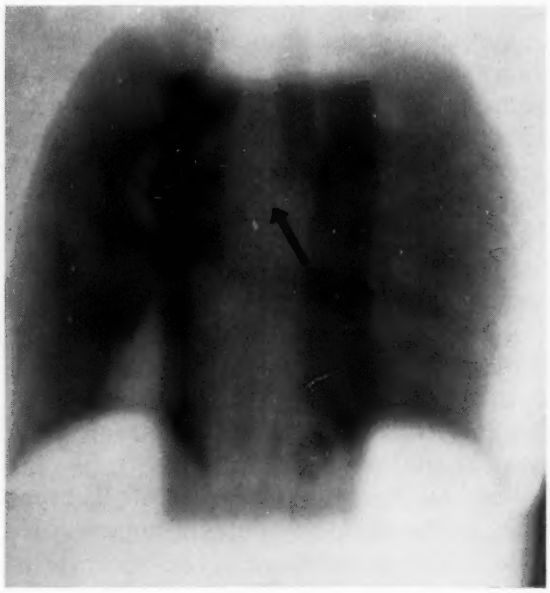

FIG. 3. Sides reversed. Treatment port for carcinoma of esophagus. Previously unsuspected tumor infiltration of the left main stem bronchus is demonstrated.

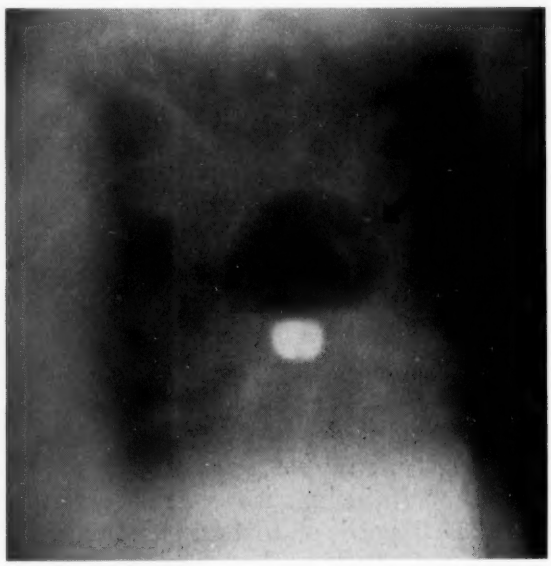

FIG. 4. Cobalt 60 radiograph showing localization of bladder for rotational therapy. Note the irregularity of the anterior wall of the bladder indicating tumor infiltrations.

Fig. 5. Cobalt 60 radiograph showing normal anatomic structures in the head and neck.

Fig. 7. Cobalt 60 radiograph showing extensive irregular carcinoma of the nasopharynx. It was necessary to include the spinal cord in the treatment field in order to cover widespread cervical metastases.

almost completely outlined by the injected air and a proper port is easily found. Very frequently, the lesion itself is seen indenting the air shadow. In Figure 4, the carcinoma is seen producing an irregularity of the anterior wall of the bladder.

One of the most important uses of cobalt 60 radiography is in the delineation of ports for treatment of lesions of the head and neck. Figure 5 demonstrates the normal anatomy of this region on a cobalt 60 radiograph. The absence of bone shadows enhances the soft tissue and air shadows and allows easy interpretation of any abnormal shadow.

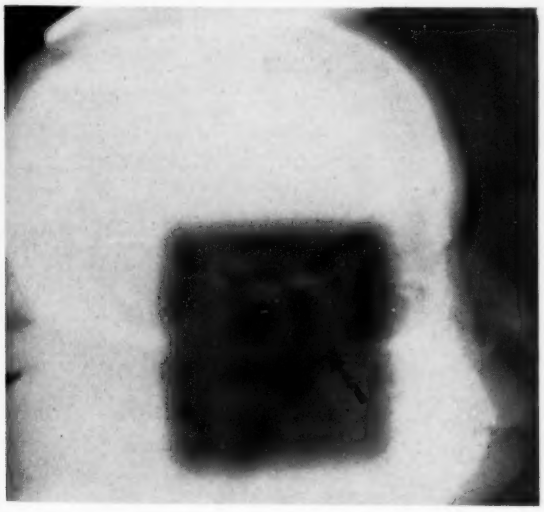

Fig. 6. Cobalt 60 radiograph showing a large neoplasm occupying all of the nasopharynx. The treatment port is seen to be too large.

Figure 6 demonstrates a neoplasm of the nasopharynx. It is seen to occupy almost all of the normal air shadow visible in the nasopharynx. The port itself is slightly large and extends too far posteriorly. This was corrected during the course of treatment. In routine treatment, port radiographs are frequently taken in order to make certain that the cervical spinal cord is not included in the treatment field unless absolutely necessary. Figure 7 shows a carcinoma of the nasopharynx that is irregular and extends almost to the posterior margin of the soft palate. The spinal cord is included in the treatment port since metastatic lymph nodes were present in the posterior cervical triangle.

In Figure 8, a treatment port for carcinoma of the soft palate is demonstrated. In this case, too much normal mouth tissue

FIG. 8. Treatment port for carcinoma of soft palate. The field size is improper. The lesion is not demonstrated, but the radiograph shows normal structures in the head and neck.

would be irradiated needlessly and the port is improperly centered. The radiograph

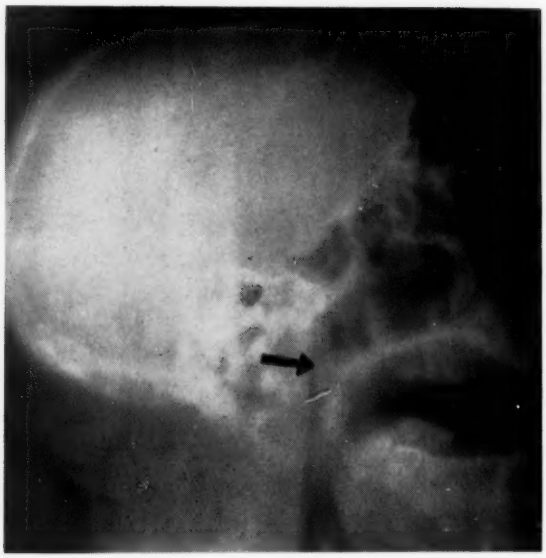

FIG. 10. Cobalt 60 radiograph showing posterior extension of the shadow of the soft palate. This proved to be a carcinoma of the soft palate.

does not show the lesion since this was a superficial growth. It demonstrates normal anatomy, and the shadow of the epiglottis is especially well visualized.

Figure 9*A* is a cobalt 60 radiograph demonstrating an irregularity of the shadow of the epiglottis which proved to be a car-

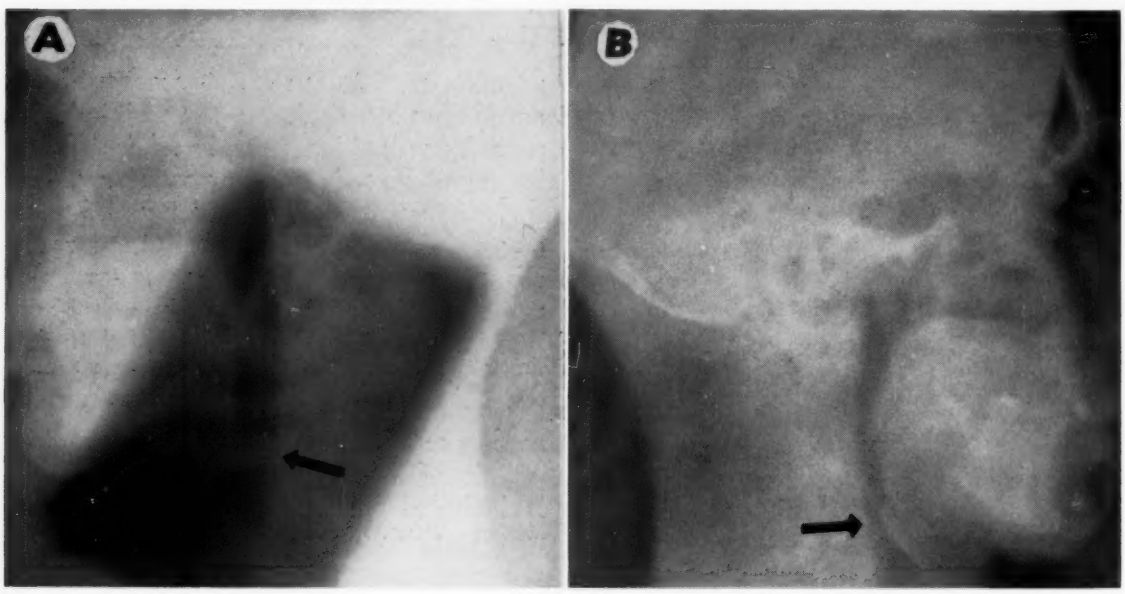

FIG. 9. (*A*) Cobalt 60 radiograph demonstrating a carcinoma of the epiglottis. (*B*) The same patient after a course of cobalt 60 teletherapy.

Fig. 11. Cobalt 60 radiograph demonstrating the fossa of Rosenmüller. This is generally not as well visualized unless the structure is edematous.

cinoma of this structure. Because of a very active otolaryngologic service, we frequently do diagnostic radiography of the head and neck, and small lesions are sometimes demonstrated that are not as apparent in patients difficult to examine by means of indirect laryngoscopy. Figure 9*B* shows the same patient as in Figure 9*A* following a course of cobalt 60 teletherapy.

A carcinoma arising from the posterior surface of the soft palate is well demonstrated in Figure 10. This patient complained of pain in the palate and the lesion was easily palpable by digital examination.

Figure 11 is of a patient who complained of partial deafness. Two biopsies of the nasopharynx were reported as normal tissue. The patient had a cobalt 60 radiograph taken and the structures of the fossa of Rosenmüller were well delineated. We have not found this in routine studies unless the patient was symptomatic and have

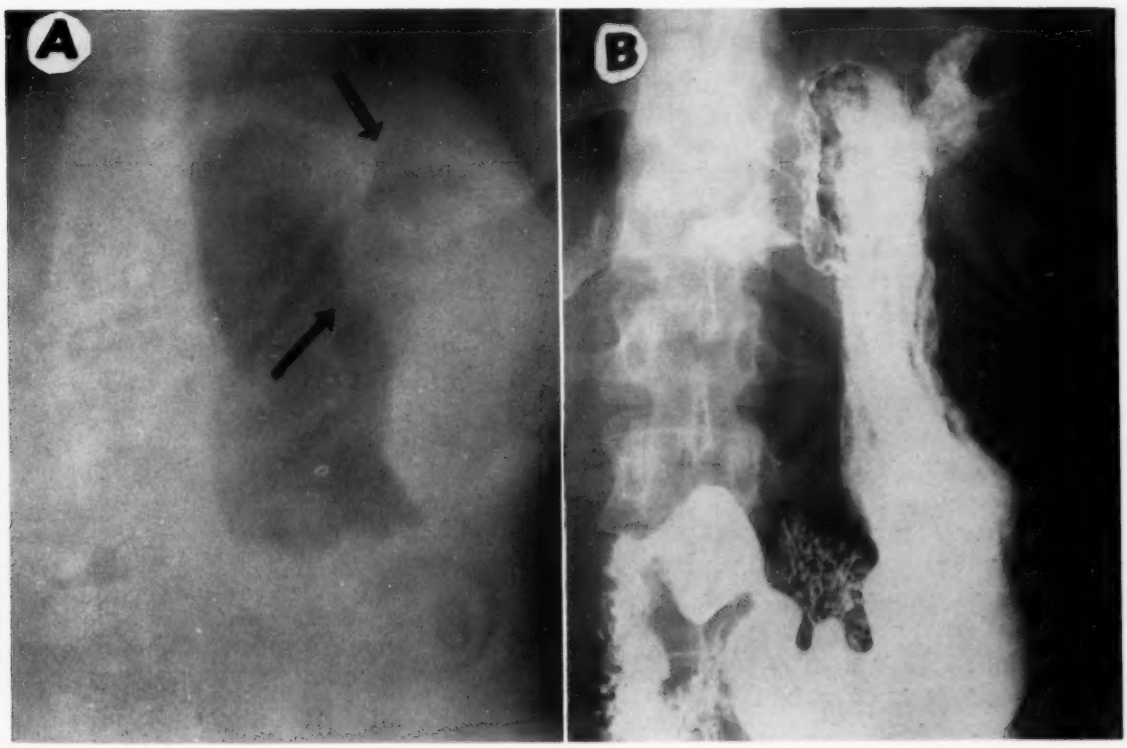

Fig. 12. (*A*) Cobalt 60 radiograph demonstrating tumor infiltration of the stomach with ulceration. Air was used as contrast material to outline the lesions. (*B*) Barium filled stomach shows the ulceration, but tumor infiltration is not well demonstrated.

concluded that edema secondary to infection or neoplasm may increase the prominence of this structure so that it becomes visible. This patient's symptoms improved following anti-inflammatory treatment.

In Figure 12*A* the cobalt 60 radiograph shows an extensive Hodgkin's disease deforming the fundus of the stomach. A large penetrating ulcer is seen extending upward and laterally from the greater curvature. This radiograph was made after partial treatment by cobalt 60 teletherapy. A previously made routine upper gastrointestinal series showed two ulcerations (Fig. 12*B*) but did not demonstrate the tumor infiltration as well as did the cobalt 60 radiograph. The ulcerations disappeared after completion of cobalt 60 teletherapy.

SUMMARY

Cobalt 60 radiography is a simple and accurate method which should be used routinely for localization of all cobalt 60 teletherapy ports.

When this technique is employed, additional information may be obtained regarding the extent and location of soft tissue lesions.

C. Richard Perryman, M.D., D.Sc. (med.)
Department of Radiology
Mercy Hospital
Pittsburgh 19, Pennsylvania

The authors wish to express their gratitude to John G. Fox, Ph.D., John C. Evans, M.D., and Wang Yen, M.D., all of whom contributed greatly to the work being reported.

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THE MOVING-STRIP TECHNIQUE IN THE ROENTGEN TREATMENT OF CARCINOMA OF THE BREAST*

By F. BATLEY, M.B., Ch.B., D.M.R.T.,† *and* A. F. HOLLOWAY, Ph.D.‡
KINGSTON, ONTARIO, CANADA

IN THE treatment of carcinoma of the breast, the radiotherapist frequently wishes to irradiate the chest wall following mastectomy to treat residual disease or local recurrence or as prophylaxis. The aim of such therapy is to treat uniformly a large area of tissue to a depth of say, 2 cm. without significant penetration to the underlying lung.

The usual method employed are not too satisfactory. A common method makes use of a parallel opposing pair of fields directed tangentially with or without bolus. The diagram in Figure 1 shows a typical arrangement. The geometric edges of the fields are indicated by the dotted lines showing that, because of divergence from the end of the cone, this arrangement is not as glancing as it might be. The diagram also indicates that, because one is using the edges of the fields, small differences in application will produce large differences in dose. If bolus bags are used, the inevitable air gaps will give additional uncertainties. Another difficulty arises from the fact that the chest wall is convex in two directions and thus the tangent pair may irradiate to a satisfactory depth in one part only to be too superficial or too deep in another.

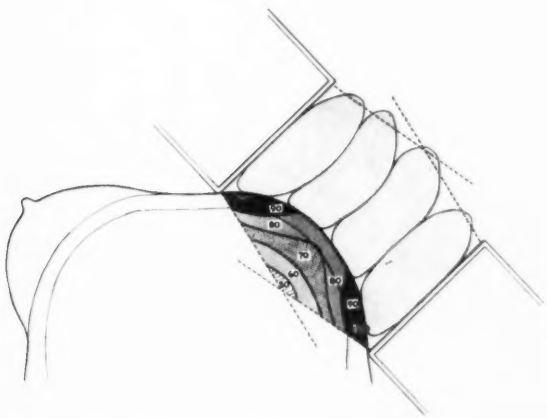

Fig. 1. This diagram indicates how a glancing pair of fields irradiates deeper than expected. The rapid change of dose at the edge shows how slight inaccuracies in positioning will significantly alter the dose received by the chest wall.

Paterson[1] has described a radium mold technique where the radium is applied at a short treatment distance. The mold accurately follows the varying contour of the chest wall, maintaining a uniform skin dose. Because of the short source skin distance, the depth dose falls steeply and thus the dose delivered to the underlying lung is small. This technique requires about 150 mg. of radium; therefore, the exposure to personnel can be high unless a careful drill is used in preparing and applying the mold. Moreover, few centers have this quantity of radium available. However, this is a most effective method.

We have devised a method using superficial roentgen rays to imitate the dose gradient delivered by the mold. One cannot treat a large area by a single field—the dose would fall off at the edges and, as the chest wall is convex, there would be additional reduction in dose towards the periphery. One way around this difficulty would be to divide the area into smaller zones, treating each separately as a patchwork. This is not attractive because of the risks of overlap or gaps. Paterson[1] described a moving strip technique by which these errors are avoided when treating a large volume. This method can be modified

* From the Ontario Cancer Foundation, Kingston, Ontario, Canada. Presented at the Forty-first Annual Meeting of the American Radium Society, Hot Springs, Virginia, April 6–8, 1959.
† Radiotherapist. Present address: Syracuse Memorial Hospital, Syracuse, New York.
‡ Physicist.

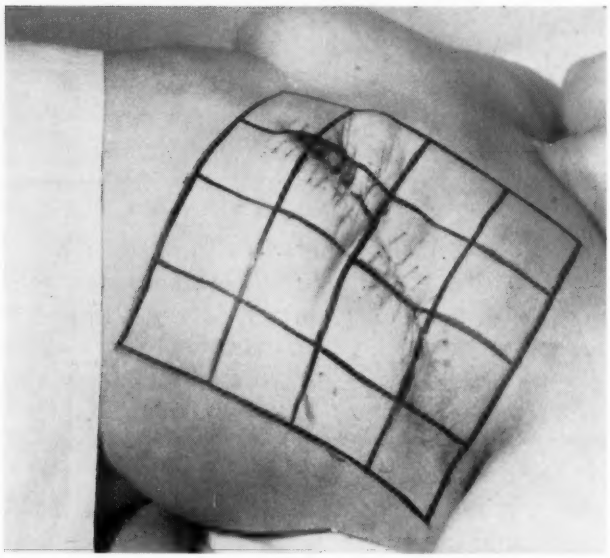

Fig. 2. Chest wall marked out for irradiation.

Method A

A	B	C	D
H	G	F	E
I	J	K	L
P	O	N	M

Chart 1. The area marked out on the patient shown in Figure 2 is lettered (see text).

in the manner described below to treat a large area such as the chest wall.

MOVING STRIP TECHNIQUE

Method A. The whole area is divided into 5 cm. squares as shown on the patient in Figure 2. However, let us imagine this area flattened out as shown on Chart 1. Square A is first treated alone, shielding the surrounding areas with lead foil. A-B are next treated, shielding off the rest as before. Next B-C are treated, then C-D. This row is completed by treating D alone. Those familiar with the moving strip technique will realize that the first row has been treated, "rolling-on" at A and "rolling-off" at D.

This procedure is now developed further by treating D-E, then D-E-C-F. Next C-F-B-G and so on finishing this row with A-H. Each square in the first row has now been treated four times and only at two of these could any overlap or gap be present. This first row is now omitted, the next exposures consisting of H-I, H-I-G-J, G-J-F-K, F-K-E-L, and E-L. The whole system is shown in Table 1 and it will be noted that one "rolls off" the final row as one "rolls on" the first row. It will be appreciated that although the whole area is 20×20 cm., no treated area is larger than 10×10 cm., and over this area the dose is uniform. It will also be noticed that during the process the applicator follows the convexity of the chest wall delivering a uniform skin dose. The required penetration can be achieved by choosing suitable filtration. Figure 3 shows a photograph of the special applicator used to facilitate setting up. A perfectly uniform reaction over the whole area is obtained, a surface dose of 4,500 r in four weeks, giving a deep erythema sometimes

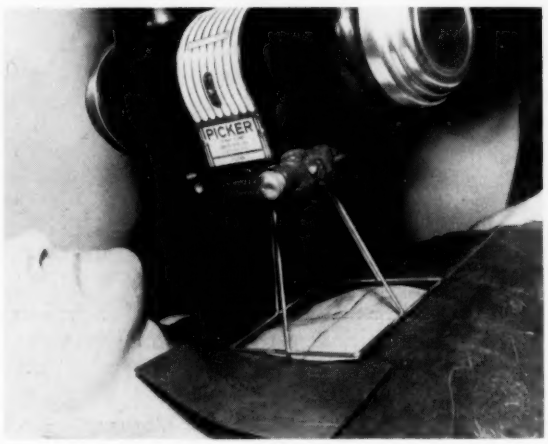

Fig. 3. Photograph showing a treatment area shielded off to 10×10 cm. with special applicator in place.

TABLE I

METHOD A—TREATMENT SCHEME
DAILY TREATMENT: 25 FIELDS

Field No.	Area	Field No.	Area	Field No.	Area	Field No.	Area	Field No.	Area
1	A	6	D-E	11	H-I	16	L-M	21	P
2	A-B	7	D-E-C-F	12	H-I-G-J	17	L-M-K-N	22	P-O
3	B-C	8	C-F-B-G	13	G-J-F-K	18	K-N-J-O	23	O-N
4	C-D	9	B-G-A-H	14	F-K-E-L	19	J-O-I-P	24	N-M
5	D	10	A-H	15	E-L	20	I-P	25	M

proceeding to moist desquamation. During the fourth week of treatment the dosage is sometimes adjusted, depending on the degree of erythema which has appeared. Figure 4 shows a patient treated for skin recurrences, demonstrating the uniform moist desquamation which can be achieved. This patient was unusually sensitive and treatment was stopped when 4,000 r had been delivered, the photograph being taken ten days later. Figure 5 shows the same patient four weeks after completion of treatment, indicating that rapid healing is taking place. In Figure 6 the area is shown six months after the treatment, well healed. It is now a year since her therapy and roentgenograms of the chest have shown no lung or pleural reaction.

This method consisting of twenty-five exposures each day is probably too time-consuming for most departments. Method B is a quicker alternative, which has become our standard technique.

Method B. In this the whole area, marked out as before, is again treated daily but in a much easier manner. On the first day the large square A-B-G-H (Chart 2) is first treated as one field, then C-D-E-F and the two other large squares K-L-M-N and I-J-O-P are also treated, matching up this patchwork neatly. On the second day the central large square G-F-K-J is treated followed by the areas H-I, B-C, E-L, and

FIG. 4. Photograph showing the uniformity of the reaction. This was taken ten days after completion of treatment.

FIG. 5. The same patient as shown in Figure 4, four weeks after completion of treatment. Rapid healing is taking place.

Method B

A	B	C	D
H	G	F	E
I	J	K	L
P	O	N	M

Areas treated on odd days.

A	B	C	D
H	G	F	E
I	J	K	L
P	O	N	M

Areas treated on even days.

CHART 2.

O-N. Finally the four corner squares A,D,M,P, are treated. On the third day the first day's treatment is repeated, and so on, alternating treatments from day to day. The complete area is treated daily, as before, and the required dose is similar to that for Method A. The possibility of overlap or gaps at the edges of the fields can occur only during half of the treatments, the chance being the same as with Method A.

Figure 7 shows how an irregular area is marked out for treatment. The regular pattern is fitted over it, and the excess portions are shielded throughout the treatment, which is carried out in the usual fashion according to either method.

With both techniques, uniform consistent reactions have been obtained. This allows the dose to be carried to a high level, whereas in techniques where inaccuracies are common, attempts at high dosage are hazardous.

FIG. 6. The same patient as shown in Figures 4 and 5, six months after treatment.

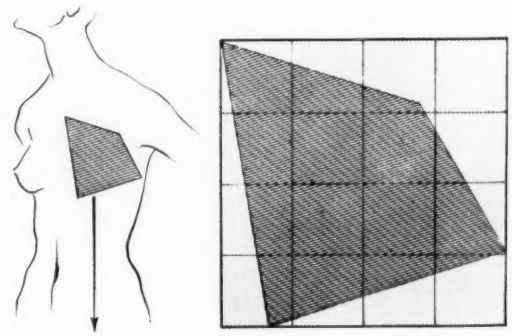

FIG. 7. Diagram indicates how an irregular area is marked out for treatment.

PHYSICAL FACTORS

Treatments were carried out using a superficial roentgen-ray machine under the following conditions: focal skin distance, 20 cm., 100 kv. peak, 10 ma. with 1 mm. Al added filter, the half value layer being 2 mm. Al. With these factors the percentage depth dose in unit density soft tissue is 75 per cent at 1 cm. and 56 per cent at 2 cm. for a 10×10 cm. field, if the treated area is a plane. However, when the curvature of the chest and the low density of lung tissue are allowed for, it appears that under the above conditions the percentage depth dose in the lung at 5 cm. below the skin is in the order of 65 per cent. Thus, with a surface dose of 4,500 r there would be a dose gradient to 3,000 r at 5 cm. depth. Although no lung damage has yet been observed with this technique, we are considering the use of a less penetrating beam, using the physical factors listed above with no added filter. By this means the half value layer is reduced to 0.8 mm. Al on our machine, and the dose to the lung would then be approximately 35 per cent at 5 cm. below the skin.

SUMMARY

Treatment of the chest wall for breast cancer requires uniform irradiation of a large area of tissue with minimum penetration to the underlying lung. This can be achieved by superficial roentgen therapy using multiple small fields. Two methods have been described by which the effect of possible overlapping or gaps can be avoided. Superficial skin carcinomata, extending over a wide area such as is sometimes seen on the scalp, can be treated with the same techniques.

F. Batley, M.B., Ch.B., D.M.R.T.
Ontario Cancer Foundation
Kingston Clinic
Kingston, Ontario, Canada

We wish to thank Dr. Collins, who discussed this paper at the American Radium Society Meeting, for pointing out the possibility that the curvature of the chest wall would increase the dose to lung more than one would expect from a study of the standard isodose pattern.

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RADIATION THERAPY OF BENIGN CONDITIONS*

By GEORGE COOPER, Jr., M.D.
CHARLOTTESVILLE, VIRGINIA

VERY soon after their discovery in 1895, roentgen rays were put to practical use by physicians. Acute radiation reactions, the local and systemic effects of large doses delivered in a short time, promptly manifested themselves and, in due course, their sequelae appeared. By 1920, radiologists had been forcefully taught the cumulative effects of repeated small doses of ionizing energy by changes in the skin of their own hands. That minute amounts of radiation might produce significant after effects was, however, not widely appreciated until about 1945. By then, the potential significance of Muller's demonstration that radiation of the gonads speeds up the rate of mutation loomed alarmingly; and since then, among other worrisome reports, data correlating the increase in the incidence of leukemia[6,12] and of carcinoma of the thyroid[14] with small or minute doses of radiation have been especially disturbing. Dr. Shields Warren's 1956 paper,[15] *Longevity and Causes of Death from Irradiation in Physicians*, gave radiologists in particular food for uneasy thought. Happily, the impact of much of these data on the leukemogenic, carcinogenic, and premature aging effects of minute quantities of ionizing energy has been softened by statistical re-evaluation. Furthermore, a growing realization that radiation is not the only mutagenic agent to which man is exposed and the fact that "chemical subtances outside of biological experience"[2] are produced by industry and modern medicine are diffusing the spotlight which has been so glaringly concentrated on radiology. Recent reports from the Russells[4] have been especially heartening. They have published data indicating that there is no strict linearity between cumulative radiation dosage and mutation rate in the spermatogonia of mice, and that the mature egg cells in the mouse are more radioresistant than its spermatogonia.

Nevertheless, the field under review has been affected by the accentuated awareness of radiation hazards. Near hysteria has led to sweeping statements condemning the use of radiation therapy for benign conditions under any circumstance.

This attitude has been fostered by cursory reading of reports such as the leading article in a recent issue of the *New England Journal of Medicine*,[3] in which three surgeons presented an excellent review of the patients seen at the Massachusetts General Hospital who had sustained severe injury from irradiation for a benign condition. Therapeutic radiologists are grateful to have physicians in other fields point out that "irradiation for benign conditions may produce tissue changes more disabling than the original condition for which the x-rays were administered," and that bad results "suggest that those not fully qualified in the therapeutic use of x-rays should be excluded from the application of this potentially dangerous tool." When written by radiologists, this conclusion receives less attention. Unfortunately, the superficial reader fails to distinguish between poor radiation therapy and good radiation therapy, and draws the unwarranted conclusion that irradiation for benign conditions should be condemned rather than the physician who employs radiation carelessly and ignorantly. It would be as logical to condemn the use of surgery in conditions not posing an immediate threat to life because some surgeons, not thoroughly qualified to perform the procedures they undertake, get bad results.

Scientists should be able to evaluate objectively this question: How has the

* From the Department of Radiology, University of Virginia Medical Center, Charlottesville, Virginia. Presented at the Sixtieth Annual Meeting of the American Roentgen Ray Society, Cincinnati, Ohio, September 22–25, 1959.

greater understanding of radiation hazards affected the indications and contraindications for, the dosimetry and techniques of, irradiation in benign conditions?

CELLULITIS, FURUNCLES, CARBUNCLES[9]

History. The value of small doses of radiation in the treatment of infection became generally recognized during the 1920's. Radiation was used in a wide variety of inflammatory conditions for approximately the next fifteen to twenty years. In the late 1930's, the sulfa drugs were introduced, and in 1944 the large scale production of penicillin commenced. Since then, a host of drugs and antibiotics has almost eliminated radiation in medical thinking about infection; but there is now reason to reopen the subject.

With the passing of the years, the widespread and often unnecessary administration of chemicals has produced two thoroughly unpleasant results. The organisms responsible for the infections have, by a process of natural selection, developed resistant strains faster than new agents can be devised, and people have become sensitized to the agents. Our medical journals report account after account of drug reactions and of infections by drug resistant organisms. In 1959, at the annual meeting of the American College of Physicians, Dr. Maxwell Finland of the Boston City Hospital reported some as yet unpublished but thought provoking statistics collected in the Boston area. Among other findings, these show that the total number of patients with positive blood cultures has risen steadily through the entire period, 1935 through 1957. Following the introduction of the sulfa drugs and penicillin, there was an initial sharp drop in the percentage of deaths in people with positive blood cultures, then a leveling off, and, for approximately the last decade, an accelerating rise. The curve for all organisms, exclusive of *Staphylococcus albus*, closely paralleled the curve for *Staphylococcus albus* alone.

The lesson to be learned from this and other reports is plain. The use of these valuable materials should be reserved for time of real need, to fight infections which threaten to cripple or kill. There is now a growing appreciation of the fact that every time an infection is overcome without them, the chance of successfully combating a subsequent more severe episode in the same patient is increased, and that, conversely, every time the materials are given unnecessarily, the future of the patient is jeopardized. But the part that radiation can play in reducing their use is too often ignored.

Mechanism of Action. In spite of a great deal of experimental work, many questions about how radiation influences infections have never been fully answered. However, it seems quite definite that there is no direct bacteriocidal action from the small doses which contribute most effectively to the handling of infections. Neither does it seem possible that radiation increases antibody production by a direct effect on the body's immunologic response. The improvement which follows is probably due to the action of ionizing energy on the cellular exudate accompanying the inflammation and on the capillary bed.

After even small doses, the disintegration of lymphocytes commences in as little as fifteen minutes, while polymorphonuclear leukocytes and eosinophils begin to break down in a few hours. As these cells are present in large numbers in infections, the release of their products may be assumed to destroy bacteria and stimulate phagocytosis by other cells, which flood in to replace the ones destroyed by the radiation.

Small doses of radiation are also followed by dilatation of the capillary network in the irradiated tissue, which results in the warmth and throbbing sensation which often occur about six hours after exposure. It seems logical to assume that the increased blood flow carries away toxins and debris at an accelerated rate. As radiation also causes swelling of endothelial cells and increased permeability of vessel walls, the cells and fluid can pass more readily from the capillaries into the tissues, and the re-

moval of toxins and debris is made easier.

The Value of Irradiation. Whatever the exact mechanism of its action, roentgen therapy is an adjunct of proved value in the treatment of many infections. It is a nonspecific form of treatment which merely stimulates the natural defenses of the body. It does not sensitize the patient, and it does not lead to the development of bacterial strains with which it is more difficult to cope. The number of cases of cellulitis, furuncles, and carbuncles that can be cleared up by rest, hot compresses, and indicated surgical drainage would surprise younger physicians who have entered practice since the use of antibiotics and chemotherapy has become rampant. The judicious supplementation of these simple measures with roentgen therapy helps to abort or localize many of the more threatening or stubborn infections. In the truly difficult cases, antibiotics or chemotherapy are, of course, needed, but even in these cases the use of radiation can reduce the total amount of drugs or antibiotics given.

Cultures should be obtained prior to any therapy. Then, during the period of treatment with the simple agents (which includes roentgen rays), the identity of the organism and its sensitivity to various antibiotics can be determined. While using nonsensitizing agents to which the organism will not become resistant, the physician can gain information with which to choose his chemotherapeutic agent wisely. If the infection subsides without chemotherapy, he will not need the information but, if the infection proves stubborn, he can use an agent known to be effective against the responsible organism.

Technique. The technique of roentgen therapy is simple. The infected area and a margin should be exposed. The less localized the infection, the wider should be the included margin. The tissue peripheral to the area which is to be exposed should be shielded with sheet lead or lead rubber, and the major portion of the rest of the body covered by a lead rubber apron or lead fiberglass sheet. The exposure should then

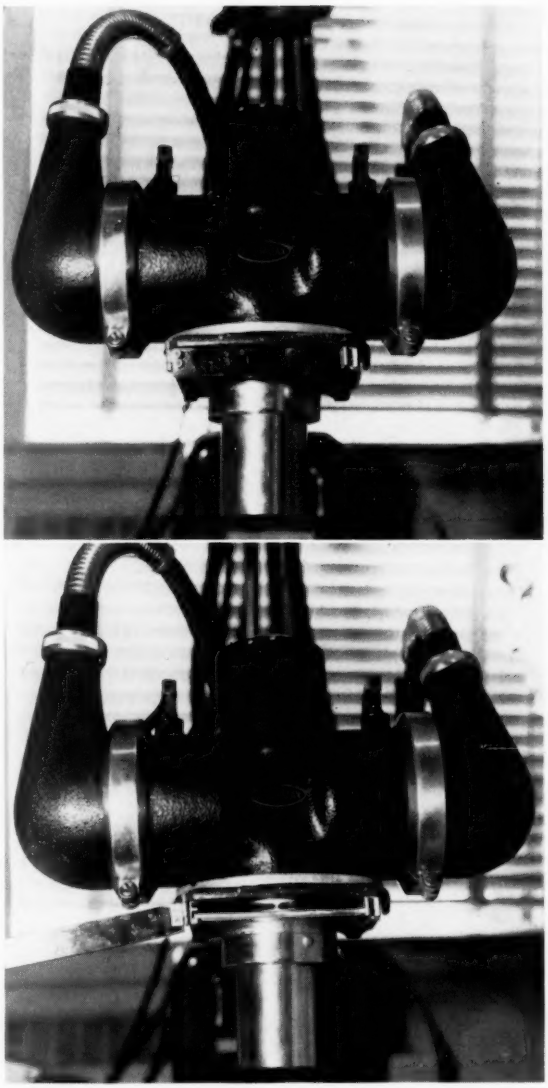

Fig. 1. This standard low voltage roentgen therapy unit contained a leak which was easily corrected by attaching a shutter which can be closed over the leak.

be made through a cone that is no larger than necessary and closely approximated to the skin surface. This degree of protection is perhaps superfluous since the amount of total body and gonadal irradiation avoided is too small to measure. But there are three good reasons for making this a routine procedure. First, so many uncertainties still surround the subject of the effect of radiation on tissue that no precaution should be considered excessive. Secondly, full body shielding guards against

undetected equipment defects (Fig. 1). Thirdly, most people today are acutely aware of radiation hazards; full protection inspires confidence in their radiologist.

If the infection is near the thyroid gland or gonads, these structures should be shielded with special care. The younger the individual, the more careful should be the shielding, and the very young should be treated under only exceptional circumstances, if at all.

Dosimetry. Small doses only are needed. In acute infections, 100 to 150 r in air is given at the first treatment. A second dose of 75 to 100 r forty-eight hours later is often necessary, and occasionally a third exposure of 75 to 100 r four or five days later. In chronic infections, an initial dose of 150 r is followed by doses of 75 to 100 r once a week for three to four treatments. In unusually stubborn infections, such as a chronic axillary furunculosis, up to eight treatments may be advisable.

In most lesions, a half value layer of 1.8 mm. Al suffices, though some carbuncles are so deeply indurated as to require 0.35 mm. Cu.

Results. It is interesting to note that from July 1, 1956 to June 30, 1957, we treated only 4 patients suffering from a cellulitis, furuncle or carbuncle and just 3 from July 1, 1957 to June 30, 1958. From July 1, 1958, to June 30, 1959, these cases numbered 15, the most since 1946. Of course, in this same year, we also used radiation therapy in a larger number of many varieties of carcinoma, but it does appear that at least some physicians are beginning again to take advantage of the usefulness of roentgen therapy in infections.

Because it is not possible to predetermine the course of a particular lesion with and without roentgen therapy, exact comparison of results cannot be made, but the clinical conviction is overwhelming—a gentle prodding of the body's defense mechanism with small doses of roentgen rays is effective. Properly carried out, the procedure is safe and is a more conservative measure than the use of chemotherapy or antibiotics.

TUBERCULOUS CERVICAL LYMPHADENITIS

To a greater degree than most other infections against which irradiation at one time was a major defense, tuberculous cervical lymphadenitis is handled successfully by drugs, such as isoniazid and para-aminosalicylic acid. Many open cavity cases of pulmonary tuberculosis become drug resistant but few of tuberculous cervical lymphadenitis. However, that the drug resistant cases are few does not decrease the value of roentgen therapy in those cases. We have been asked to help with only 2 cases in the past three years, but in these 2 individuals irradiation was followed by regression of involved lymph nodes which had remained stationary under persistent drug therapy.

Small amounts of radiation are effective. Usually from four to eight treatments of only 100 r air dose with a half value layer of 1 to 2 mm. Al, given at weekly intervals, is all that is necessary. The shielding should be arranged so as to expose the smallest possible skin area. Particular care should be taken to minimize thyroid gland exposure, and it is good practice to protect the trunk. The younger the patient, the more persistent should be the effort to control the disease without the help of irradiation.

CHRONIC SINUSITIS, AND CHRONIC LYMPHOID FOLLICULITIS AND HYPERPLASIA[8]

Among the many infections that were treated frequently with roentgen therapy in the period between 1925 and 1940 were those in the upper respiratory tracts of children. The greater efficiency of chemotherapy and antibiotics in the treatment of these conditions and the desirability of avoiding radiation exposure in the young combine to make roentgen therapy of acute infections in the upper respiratory tracts of children a subject of historic interest only; but with the increasing capacity of the bacteria in our environment to tolerate our drugs, chronic infections in this region occur more frequently and deserve some discussion. Chronic mastoiditis, and chronic

tonsillitis and adenoiditis with or without hyperplasia are usually terminated surgically. Chronic sinusitis, and chronic lymphoid folliculitis and hyperplasia are not so easily managed, yet failure to correct them may lead to deafness, asthma, and bronchiectasis. In children who have chronic sinusitis or chronic lymphoid folliculitis and hyperplasia, and early evidence of one or more of these complications, the potential hazard of the developing complication far exceeds the hazard involved in carefully administered, small doses of radiation. As the child grows older and as the sinuses and their ostia enlarge, sinusitis usually becomes less of a problem and lymphoid follicles regress. Roentgen therapy may give relief which will help the child get through a difficult period in its growth and development without permanent disability.

RADIATION THERAPY IN CHILDREN

Chronic Sinusitis. Irradiation of the sinuses helps in two ways. It bolsters the natural defense mechanism against infection and it thins the swollen hyperplastic membranes, permitting better drainage.

In children, the frontal and sphenoid sinuses are rarely a major site of infection. Usually, after consultation with the otorhinolaryngologist and a study of the roentgenograms, it is decided to treat the antra alone or to include the ethmoids.

In treating only the antra, a cut-out should be made in lead or lead rubber shielding which covers the entire face and neck with the opening just large enough to expose one antrum. Treatment should be given through a round cone which includes the cut-out only and which is brought into close approximation to the shielding. The trunk should be shielded. The quality of the beam should be such as to ensure a reasonable depth dose at the level of the posterior wall of the antrum, that is, a half value layer of 2 to 4 mm. Al. Fifty to 100 r in air may be given to each antrum two or three times a week for a total air dose of 200 to 600 r to each antrum. The exact dosage and the number and frequency of exposures should be determined by the patient's age and response.

When the decision is to treat the ethmoids as well as the antra, the facial shielding is more difficult. It is usually best to expose the antra and the bridge of the nose simultaneously. The neck and the rest of the face must be fully shielded, and particular care should be taken to protect the eyes and brows. The dosage is essentially the same as when only the antra are irradiated, except that with irradiation of a larger block of tissue a somewhat smaller total air dose is usually needed.

Chronic Lymphoid Folliculitis and Hyperplasia. The local application of radium may be preferred when one or two lymph follicles obstruct the eustachian tube orifices. When hyperplasia and infection are diffused throughout the pharynx, roentgen therapy is often helpful and should be considered when the otorhinolaryngologist has exhausted his other resources and when the child's hearing or general condition is in jeopardy. When a lateral portal just large enough to cover the pharynx is exposed and the rest of the head and neck are shielded, thyroid irradiation is reduced to minute amounts of scatter. The trunk should be shielded also. The half value layer selected depends on the thickness of the child's face and will usually fall in the 4 to 8 mm. Al range. It is perhaps preferable to give an air dose of 50 to 150 r to one portal only, then to give the opposite portal the same dose forty-eight hours later; but both portals can be treated at one sitting with only an occasional, moderate accentuation of symptoms. The procedure is repeated at intervals of one to three weeks for a total air dose to each side of 200 to 900 r. The dosage per treatment, the interval between treatments, and the total dosage are individualized to suit the patient and his response.

Again there is a twofold benefit. The body's defense against the local infection is augmented and hyperplastic tissue is reduced.

Indications for Irradiation. It is empha-

sized that radiation therapy for both chronic sinusitis and chronic lymphoid folliculitis and hyperplasia should be used only when persistent use of other measures has failed and when the child develops or is in danger of developing deafness, asthma, or bronchiectasis. The situation is not encountered often but, when it is, radiation therapy may be of real value.

In the last three years, we have treated only 3 of these patients. All of the children were about five years old, had chronic sinusitis and early asthma, and received only 300 to 500 r air dose to each antrum. Both the sinusitis and the asthma regressed nicely in all 3 of these children. They have had recurrence of sinusitis, but not prolonged, and, so far, no return of the asthma.

RADIATION THERAPY IN ADULTS[13]

In treating chronic sinusitis, often following the first exposure and sometimes after subsequent exposures, irradiation is followed by a more profuse nasal discharge. In a patient who has an elevated temperature, sinus pain, headache, asthma or other symptoms, there is frequently an exacerbation. This observation may be used to advantage in the recognition of subclinical sinusitis in adults in whom sinus infection is suspected but not proved by the ordinary means. The patients are usually individuals suffering from hay fever or asthma in whom the rhinologist has found no significant evidence of sinus infection but whose hay fever or asthma has responded poorly to prior management. The antra and ethmoids may be given a single test dose of 200 r in air (half value layer of 1 mm. Cu) using the same technique as that described in the treatment of chronic sinusitis in children. When this is followed in twenty-four to seventy-two hours by a purulent nasal discharge, exacerbation of hay fever or asthma, troublesome cough, headache, or malaise, comprehensive treatment for sinusitis, which occasionally includes further irradiation, is often followed by improvement in the hay fever or asthma.

In the last three years, we have been asked by our allergists to give roentgen therapy to 3 adults with stubborn chronic sinusitis and asthma. The plan of treatment is essentially the same as in children. The ethmoids and antra are exposed; a heavier half value layer is used (1 mm. Cu); the single dose is a little larger, 125 to 150 r; and the total air dose is usually about 900 r. The results are less dramatic than in children but in the 3 carefully selected patients just mentioned, irradiation of the sinuses was followed by definite improvement of the asthma.

ACUTE AND SUBACUTE NONSUPPURATIVE THYROIDITIS

The etiology of most acute and subacute cases of nonsuppurative thyroiditis is unknown. Acute thyroiditis is observed in association with a variety of acute viral diseases, usually subsiding with recovery from the primary disease; but in some patients acute or subacute thyroiditis occurs as the primary disease. Here the course may range from slight tenderness of the thyroid gland with few systemic manifestations to a severe disturbance with marked inflammation of the thyroid gland, fever, hyperthyroidism, and later a period of hypothyroidism.

Recently, antibodies to thyroglobulin have been demonstrated in patients with several types of thyroiditis. At the April, 1959, meeting of the American College of Physicians, Doctors Witebsky, Rose and Shulman presented an as yet unpublished paper on *Autoimmunization in Thyroiditis* which adds important data. By injecting extracts of thyroid glands from various animals into other animals of the same species, these workers elicited the formation of specific thyroid antibodies. Thyroglobulin isolated from the thyroid extracts was the leading antigen. The glands of the antibody producing animals showed histologic changes closely resembling those seen in patients with nonsuppurative thyroiditis. In these cases serologic examinations frequently revealed the presence of thyroid antibodies against human thyroid extract

and human thyroglobulin.

On the basis of these various studies, it has been postulated that the inflammatory reaction in some cases of thyroiditis is an expression of the immunity response to antibodies of thyroglobulin produced when it escapes from injured acini. This interesting concept offers no clue as to the etiology of the acinar injury but suggests that any agent which causes acinar injury may trigger the chain of events.

Clinical Treatment. Rest, analgesia, and local ice packs are obviously called for. When these simple measures are not enough, antithyroid drugs would seem to provide a promising physiologic means of attack. The suppression of thyroxin output should reduce the local inflammation and, in fact, thiouracil and its derivatives have been found helpful. Unfortunately, the complex interrelations of the glands of internal secretion make it difficult, at this stage of our knowledge, to produce the specific alteration desired. Thyroid extract or thyroxin may be given to counteract the thyroid stimulating hormone mechanism, and so to rest the gland, but steroids and corticotrophin have been more effective than the antithyroid drugs. In acute nonsuppurative thyroiditis persisting for a week or so, cortisone or prednisone is usually given. The benefit that follows may be due in part simply to the anti-inflammatory effect of the steroids. The decrease in tissue response no doubt reduces symptoms. But cortisone (or prednisone) also suppresses the pituitary, which in turn causes suppression of the thyroid, and it may act on the thyroid directly as well, inhibiting the thyroid stimulating hormone mechanism and binding the thyroxin that has been extravasated into the tissues. The injured acini are thus given a chance to repair and again to retain thyroglobulin.

When steroids are not promptly effective and when withdrawing them is followed by relapse, irradiation should be used. The mechanism of its action in this condition is unknown, but its effectiveness has been thoroughly documented.

Roentgen Therapy. The dosage used should be small. Because the antibody produced in thyroiditis destroys thyroglobulin, the autoimmunization process itself leads to a hypothyroid state. Temporary hypothyroidism often occurs in people who have had thyroiditis, and myxedema is occasionally a result of the process. Radiation dosage apt to impair the functioning of the gland must, therefore, be avoided. Each side of the neck may be given 100 r in air through directly opposing portals for three to eight treatments. Sometimes only one lobe need be treated or a direct anterior portal over the isthmus may be indicated. The half value layer selected need not exceed, and usually is, 1 mm. Cu but may be less. Some radiologists prefer to treat daily. Treatment every other day seems to be equally as beneficial, and it allows fuller evaluation of the effect with the likelihood that fewer treatments will be found sufficient. In a few patients it may seem desirable to go on to a total dose of 1,000 r in air to each lobe, but generally, if 800 r does not produce a good result, the case probably involves unusual factors calling for further evaluation rather than more irradiation.

The cases which come to irradiation are those which have not yielded to steroid therapy. They are the stubborn cases, and a significant number of recurrences should be expected, 15 to 30 per cent. A second similar course of roentgen therapy may be given for recurrence. Continued difficulty should lead to suspicion of unrecognized trouble, and the cessation of roentgen treatment.

As there is a possibility that small amounts of radiation over the thyroid in infancy and childhood may increase the incidence rate of carcinoma of that gland, the radiologist should resist requests for radiation treatment of thyroiditis in the very young. Fortunately most cases occur in the fourth and fifth decades, and the benefit of wise use of small doses of irradiation for thyroiditis in adults far exceeds the somatic hazard.

The irradiated field should be no larger

than necessary to cover the inflamed tissue. Irradiation should be confined to the desired field by use of the smallest possible cone and careful shielding. As the cone cannot always be brought into snug apposition with the rounded neck, attention to shielding is especially important, and should be extended to include the entire trunk.

Our own experience with thyroiditis has been satisfying. In the five year period, 1954 through 1958, we treated 10 cases in which we have complete follow-ups. One of the patients had a second course of irradiation for recurrence. All are now well and have normally functioning thyroids. Two of the patients received only 300 r. One of these was the patient who suffered recurrence. She was given a second course of 300 r. One patient received 1,000 r, and 1 was given 800 r. The other 6 received from 400 r to 600 r.

In addition, we irradiated 1 patient in whom, after one treatment, a peritracheal abscess was belatedly recognized. In another individual, we stopped treatment after giving a total dose of 500 r because the complete lack of response led us to doubt the diagnosis. During the succeeding year the patient had persistent trouble and the thyroid gland became nodular. Thyroidectomy then brought relief.

WARTS

In March, 1957, with the agreement and cooperation of our Department of Dermatology, we modified our use of roentgen therapy in the handling of warts. Before that date we had been following the common practice of delivering 1,200–1,800 r in air, half value layer 1.1 mm. Cu, to the lesion in one exposure. Doses of this order are occasionally followed by skin damage, especially in the elderly, leading some radiologists to advise against irradiation of verrucae in patients over fifty years of age.[11] The possibility of skin sequelae and epiphyseal disturbance also contraindicates irradiation of verrucae in the very young. When there is only partial involution or failure after roentgen therapy, the dermatologist is handicapped in further treatment of the lesion by uncertainty as to how much more insult the skin can tolerate. The application of destructive agents to skin which has received 1,000–2,000 r may result in chronic ulceration. For these reasons, irradiation, along with surgery, is sometimes referred to as a "radical" or "drastic" means of treating warts.[5] These considerations led to the modifications in our treatment.

Modified Roentgen Therapy. The usual verruca is given 300 r in air, half value layer 1.2 mm. Al, once a week for three treatments. If the lesion is superficial, and especially if the patient is a child, a half value layer of 1.0 mm. Al is used. Some deeply penetrating plantar warts receive a fourth treatment, and some are treated with a half value layer of 1.8 mm. Al. Dead skin is pared away the night before each treatment.

This determination of dosage was influenced by several considerations: (1) the risk of radiation complications; (2) the possible effectiveness of fractionation and smaller doses, since warts respond to suggestion and psychotherapy; and (3) collaboration, not competition, with our dermatologists. We planned radiation therapy which, if it resulted in only partial involution, would not interfere with further vigorous treatment by the dermatologist.

After two years of experience with this plan, the results appear satisfactory (Tables 1 and 11). The treatment is more difficult in

Table I

VERRUCAE VULGARES

No. of Patients	No. of Warts	Results
3	Multiple warts on all fingers	Not affected in 1 patient Completely involuted in 2 patients
7	13 warts	Involuted completely
2	Lost to follow-up	
Total 12		

Table II

VERRUCAE PLANTARES

No. of Patients	No. of Warts	Results
4	6	No response to irradiation but 4 warts (2 patients) involuted under persistent medical treatment
11	13	Involuted partly and 10 of these warts (8 patients) cleared up under further medical treatment
9	14	Involuted completely
Total 24	33	

the deeply penetrating intradermal verruca plantaris than in the more superficial protruding verruca vulgaris. Of paramount importance is close cooperation between the dermatologist and radiologist. Neither one alone can accomplish as much. In fact, we recommend that the radiologist who undertakes to treat warts secure first the collaboration of a dermatologist, and that the dermatologist avoid the temptation to use roentgen therapy too freely by securing the collaboration of a radiologist.

An example of the limitation imposed by working alone is the attitude of many not to use radiation in the handling of mosaic warts because irradiation alone usually does not cause complete involution of these lesions. In our experience, irradiation makes the mosaic wart more amenable to subsequent treatment by the dermatologist.

Our present dosage schedule removes the fear of devitalizing the skin of elderly patients, and relieves much of the worry about the young patients. Included in the group reported in Table I and II are 3 patients over fifty and 2 children under ten, 1 nine and 1 seven. We have not had the slightest indication of skin damage in those patients who received irradiation only, medical treatment followed by irradiation, or medical treatment before and after irradiation.

The small fractionated dose is conservative and safe. Its administration is simple. It can be used freely in the handling of verrucae vulgares and plantares. Small doses of very soft roentgen rays can be used in verrucae planae but should rarely be needed.

Indications for Irradiation. It is recommended that irradiation be used as the initial form of therapy in subungual warts only. In others, medical measures are first given an adequate but not unduly prolonged trial. If the wart persists, radiation therapy is administered. If it still persists, the verruca is usually smaller and more superficial and can be treated medically again with greater hope of success.

Contraindications for Irradiation. Fortunately, warts in the very young usually respond to medical treatment. Because of the greater susceptibility of youthful tissues to radiation injury, the younger the child, the more determined should be the medical effort to cure the lesion, and the more reluctant should the radiologist be to participate. If, to irradiate the wart, it is necessary to direct the beam toward an epiphysis in a very young patient, he should refuse to participate.

In order to avoid a synergistic action, a wart which has been treated by local applications of any kind should be irradiated only after two weeks have elapsed since the last application.

Radiation therapy directed at curing the wart should probably not be given to an infected wart. It may be desirable, however, to use smaller doses to hasten resolution of a stubborn infection.

A wart occurring in a previously irradiated skin should not receive more roentgen therapy. If the record of previous irradiation cannot be obtained or is unclear, and the patient is not certain that the wart is outside the previously irradiated area, it is wise to refuse to treat.

Technique. A portal is cut in a piece of sheet lead large enough to protect the rest of the hand or foot. One to 2 mm. beyond the horny ring of the wart should be exposed. The smallest cone which will cover the portal should be used and it should be brought into firm contact with the lead shield so as to minimize scatter.

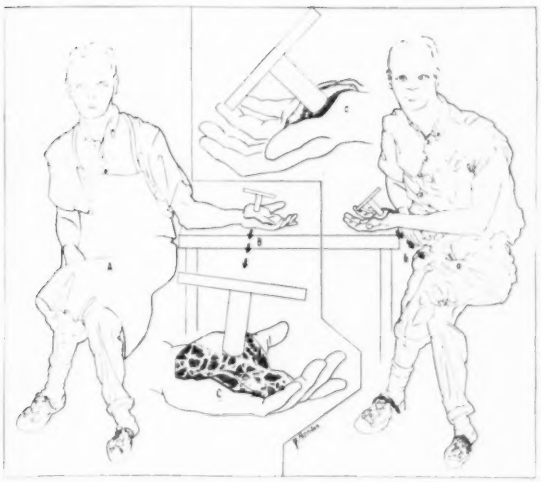

Fig. 2. In comparing protective devices when treating the hand, the area to be treated is extended away from the body with the trunk shielded (A) and the beam (B) is directed away from the body. The hand is positioned needlessly close to the unshielded trunk (a) and the beam (b) is directed toward the body. Generous shielding (C) is contrasted with skimpy shielding (c).

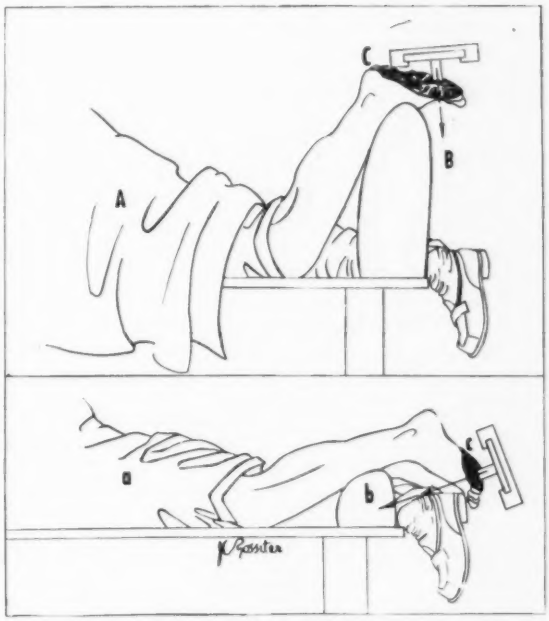

Fig. 3. Good protection of the patient when treating the foot is illustrated at the top in the protective material (A), the direction of the beam (B) and the generous shielding (C), as contrasted to a, b, and c at the bottom.

The patient should be comfortably positioned in such a way that the beam can be directed away from the body (Fig. 2 and 3), and the trunk should also be shielded.

HERPES ZOSTER

Irradiation of the posterior root ganglions often relieves the pain associated with herpes zoster. Though a high percentage of successfully treated cases is reported by several radiologists,[10] the rather slighting references to roentgen therapy in the nonradiologic literature dealing with this subject suggest that most radiologists are not consistently helpful with these patients. Four possible causes for unnecessary failure are suggested:

1. Undue attention to the skin lesions. The data reported by authors enthusiastic about the value of radiation in herpes zoster indicate that therapy should be given to the posterior root ganglions primarily, if not exclusively.

2. The use of radiation too soft to reach the depth of the posterior root ganglions. A half value layer of 1.3 mm. Cu should be adequate.

3. Insufficient number of treatments. A few early cases will be relieved after one or two exposures of 200 r as measured in air four days apart. Most require four treatments; but a few will need treatment for up to ten weeks and a total air dosage of well over 2,000 r.

4. Irradiation of too short a length of the cord. Because of the extensive overlap of adjoining dermatomes, at least two segments above and below the suspected nerve roots should be included in the field.

SUBACROMIAL BURSITIS (CALCIFICATION OF THE SUPRASPINATUS TENDON)

The subacromial bursa, the supraspinatus tendon, and adjoining structures are not the only sites of aseptic inflammation, degeneration, and calcification. Regions around bursae near the olecranon, hip, ischial tuberosity, and elsewhere may be similarly affected, but the subacromial bursa area is by far the most frequent location of this incompletely understood process.

Symptoms requiring medical attention are encountered in the middle aged and

Table III

RESULTS OF ROENTGEN THERAPY FOR SHOULDER PAIN

	No. of Cases	No Benefit 4 (22%) Showed Calcification	Moderate 24 (60%) Showed Calcification	Excellent 37 (88%) Showed Calcification
Acute (excruciating pain, less than 1 week)	18	0 (0%)	2 (11%)	16 (89%)
Subacute (severe pain, 1–3 weeks)	24	12 (33⅓%)	12 (33⅓%)	12 (33⅓%)
Chronic (moderate pain, over 3 weeks)	58	18 (31%)	26 (45%)	14 (24%)

elderly almost exclusively. Concern about hazards is, therefore, a minor factor in deciding whether to use radiation.

Review of the 100 most recent cases of shoulder pain treated with roentgen therapy, in which our records, including follow-up, are complete, produced the data in Table III.

In our experience, irradiation has the greatest chance of success when the clinical diagnosis can be confirmed by the demonstration of calcification in the roentgenogram and when symptoms are of brief duration. In acute flare-ups, the relief from excruciating pain may be dramatic. The effect is due, presumably, to absorption of inflammatory elements, with consequent relief from tension, followed by healing. Serial roentgenograms may even demonstrate partial or complete disappearance of the calcium deposits. It is logical to expect that the longer the symptoms have been present, the greater will be the irreversible tissue damage, and this expectation is borne out by the clinical results with irradiation, or any other form of therapy.

For irradiation of the shoulder, a half value layer of 1.0 mm. Cu is recommended. It is usually more comfortable for the patient to be treated sitting in a chair rather than lying on a table. In either case, a 10×10 cm. portal should be large enough, and the rest of the body should be covered by a protective garment and shields. To minimize general body absorption of radiation, the cone should be directed toward the front rather than the top of the shoulder. In deference to the proximity of the thyroid, the cone should be angled a few degrees laterally, away from that gland (Fig. 4).

In very acute cases, smaller doses at forty-eight hour intervals are helpful, but usually 150 to 200 r in air twice a week is preferable. Total dosage may conservatively range up to 1,000 r, but it is seldom necessary to exceed 800 r.

Many other methods of managing bursitis have been tried.[7] No single definitive treatment has been discovered. Probably

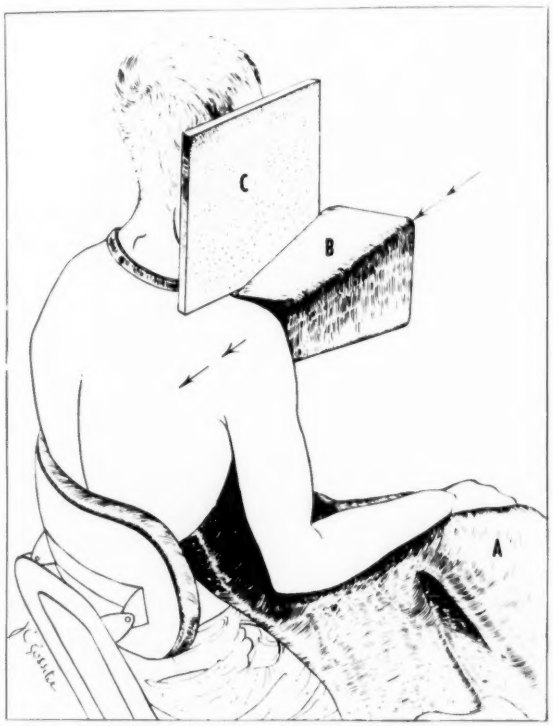

Fig. 4. The beam is directed in such a way as to minimize general body absorption and is angled slightly away from the thyroid with the head, neck and trunk shielded. (A) Protective material, (B) direction of beam, (C) protective shield.

the most widely used initial treatment today is the local injection of hydrocortisone acetate, either alone or with an anesthetic such as xylocaine or novocaine. Some prefer to try ultrasonic radiation first. Roentgen therapy may be the first, second, or third choice, depending upon the training and experience of the physician involved. It is interesting to note that only 32 per cent of the reported group of patients was referred to us by orthopedists. Recently, there has been considerable interest in the use of priscoline administered intravenously for stubborn cases.

In comparing results produced by different methods of treatments, it is important to know which treatment was used first. As most of the acute flare-ups will respond to the initial form of therapy, it is easy to misinterpret statistics. In a case in which the first method of therapy has failed, relief from any type of therapy is apt to be slow.

TINEA CAPITIS

The Kienböck-Adamson technique for radiation epilation is fully described in too many textbooks for repetition here to serve any purpose. It is suggested that to the usual safety measures be added shielding of the trunk. The procedure is exacting. Partial failures can be produced by minor errors in technique or lack of full cooperation by the patient, both of which cause some patches of the scalp to receive less than the intended amount of radiation while others receive more. An error of judgement in dosimetry can lead to incomplete or worrisomely prolonged epilation. The patients are usually school children, too young for irradiation of a benign condition to be undertaken lightly. Nevertheless, when other therapy fails, radiation epilation must be done. A new antibiotic, griseofulvin, may relieve the radiologist of this unpleasant necessity.[1] The material, which is isolated from *Penicillium griseofulvinum* and *Penicillium Janczewski*, can be given by mouth. If preliminary reports are confirmed, it causes the fungi to stop multiplying. Then, as the hair grows out, the inactive colonies can be clipped off along with the hair. Radiologists will watch experience with griseofulvin with great interest.

BENIGN SKIN DISORDERS SUCH AS ACNE AND PRURITUS ANI AND VULVAE

New forms of topical therapy, steroids, and chemotherapeutic agents are meeting most needs in these areas. If a patient suffering from one of these conditions cannot be relieved by these means, he presents an unusual problem, and it is not likely that adjunctive roentgen therapy can solve it. Consultation with or referral to an expert would be more in order.

SUMMARY

This necessarily limited presentation cannot answer fully the broad question with which it started, but certain conditions which, for one reason or another, seemed especially to deserve comment have been selected for brief review.

Advances in drug therapy have eliminated roentgen therapy in some benign conditions and have sharply reduced it in others; but it still occupies an important place in this field, and its usefulness in some conditions is increasing.

Greater understanding of radiation hazards has led the radiologist to a more meticulous technique, a more conservative dosimetry, more extensive shielding, and more discriminating selection of patients.

Indicated roentgen therapy for benign conditions can be administered without significant hazard.

Department of Radiology
University of Virginia Medical Center
Charlottesville, Virginia

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PROBLEMS IN THE PROGNOSIS OF NEUROBLASTOMA*

By HAROLD W. DARGEON, M.D.
NEW YORK, NEW YORK

NEUROBLASTOMA is one of the more common cancers of children observed on the Pediatric Service of Memorial Hospital for Cancer and Allied Diseases. From 1926 to 1958, a total of 1,498 children suffering from various malignant neoplastic diseases were admitted, 180 of whom had neuroblastomas.

The frequently peculiar, not to say bizarre, behavior of this tumor offers almost a constant challenge in diagnosis and therapy. It is the purpose of this discussion to review some experiences—of other observers as well as our own—which illustrate the difficulties in appraising the future of the patient with neuroblastoma.

MATERIAL AND RESULTS

Of our 180 cases, 108 were admitted prior to 1954. Consideration of this group of patients permits some observations on the five year or longer survivors, of which there were 15 (13 per cent).

Table I shows the age and sex of these 15 children compared with the total number seen in the same age groups. Table II shows the sites affected and the therapy used. All the usual sites of origin—cervical, thoracic, retroperitoneal, adrenal, as well as some of those less often involved, are represented among the survivors. Three of the children had disease in more than one site which was therefore multicentric in origin or metastatic. The younger age groups had the greater numbr of surevivors, but the total incidence in each age group was much too small for any accurate estimate to be made of the relationship of the age factor to curability. Surgery and irradiation was utilized in most instances, but in some it was incomplete. Chemotherapy was also used in 2 patients.

PROGNOSTIC EVALUATION

It would be erroneous to assume that the therapy employed did not contribute to the survival of the patient, but since similar measures were used in 93 other patients who did not survive, the question arises as to what factors determined the favorable prognosis in the 15 living children. Several possibilities may be considered.

1. Neuroblastoma is recognized as an embryonal tumor and has been observed to be present at birth in several instances in

TABLE I

NEUROBLASTOMA IN CHILDREN
108 CASES (1926–1953)

FIFTEEN SURVIVORS OF FIVE PLUS YEARS
BY AGE AND SEX

Age* (yr.)	Sex	Incidence Total	Survivors Total	Duration (yr.)
<1	M	4	2	12
				10
	F	8	3	8
				7
				6
1	M	8	2	18†
				6
	F	7	3	13
				8
				5
2	M	11	1	12
	F	9	1	9
5	M	6	0	
	F	6	1	11
13	M	1	1	14
	F	2	1	12

* Age on admission.
† Developed further disease at age 18.

* Presented at the Forty-first Annual Meeting of the American Radium Society, Hot Springs, Virginia, April 6–8, 1959. From the Pediatric Service and Children's Tumor Registry of Memorial Center for Cancer and Allied Diseases, New York, New York.

TABLE II

NEUROBLASTOMA

FIFTEEN SURVIVORS OF FIVE PLUS YEARS BY SITE, THERAPY, DURATION

Cases	Site(s)	Age (yr.)	Therapy	Duration (yr.)
1	Cutaneous (adrenal at 18 yr.)	1	Rd	18
1	Orbit	5	Sy Rd	11
		$\frac{6}{12}$	Sy	10
3	Cervical	13	Rd	12
		$\frac{11}{12}$	Sy	6
1	Cerv. Thoracic	1	Rd	13
1	Thoracic Epidural	2	Sy* Rd*	9
2	Retroperitoneal	$\frac{6}{12}$	Sy Rd	12
		1	Sy C	5
1	Adrenal and Liver	$\frac{6}{12}$	Sy* Rd C	8
		$\frac{8}{12}$	Sy Rd C	7
4	Lumbosacral	1	Sy* Rd	11
		1	Sy* Rd C	6
	Epidural	2	Sy	8
1	Sciatic Nerve	13	Sy	6

Sy = surgery.
Rd = roentgen therapy.
C = chemotherapy.
* = therapy incomplete.

our own series as well as by others.[5] In 1942 Potter and Parrish[4] reported the case of a stillborn fetus in which multiple neurogenic tumors were found; namely, neuroblastoma ganglioneuroma and fibroneuroma. Would not multicentricity of origin as well as metastatic disease in such an individual be a consideration? Three of our patients who likewise showed multiple sites of involvement as infants suggest the same possibility for their widespread involvement. Growths within these different sites of origin might vary depending, among other factors, on the age at which they started to develop individually either pre- or postnatally. Hence, one reason for success in the therapy of neuroblastoma which is disseminated might be in the ablation of the aggressive site (or sites) and the continued quiescence of the more "innocent" lesions; while failure could result if the malignant foci were not contained or obliterated.

2. The well-known hypothesis of Wolbach that neuroblastoma may mature into a benign tumor—a ganglioneuroma—was based on the observation of the child initially operated on at the age of two years by Stuart McGuire in Richmond, Virginia, then treated by William Bradley Coley with Coley's toxins and subsequently operated on at the age of ten by Harvey Cushing. The initial tumor was a neuroblastoma, and that removed by Cushing, a ganglioneuroma. That patient, the longest recorded survivor in the Children's Tumor Registry of Memorial Hospital, is now aged fifty years without evidence of cancer. Ganglioneuroma and neuroblastoma are not infrequently found in the same tumor removed at operation, but whether the malignant cell is therefore differentiating toward a benign process or growing concomitantly with it can only be conjectured. One of our patients (Fig. 1) showed neuroblastoma, ganglioneuroma and neurofibroma in his tumor. Despite incomplete therapy, he has survived more than ten years.

3. These neoplasms are often very vascular, and hemorrhage is a not uncommon

complication. Figure 2 shows a boy whose inoperable retroperitoneal neuroblastoma was treated by irradiation. He survived three years without local or distant extension of the tumor, but expired from a massive hemorrhage within the tumor. An infant, reported previously[3] and still living without disease at the age of nine (Fig. 3, *A* and *B*) is another example of frequent hemorrhage in a presumably metastatic case.

4. In 1956, a female child aged four months was admitted with multiple subcutaneous nodules, one of which was biopsied and showed neuroblastoma, and a very enlarged liver. The family refused any therapy and took her home against advice. Six months later the nodules began to disappear and in December, 1958, at the age of two and one-half years, she shows no signs of disease. At present this would be called a spontaneous clinical remission but we do not know whether reactivation of the recognized sites or growth of possible unrecognized sites may subsequently occur.

Fig. 1. Male, aged nine, who at birth was a paraplegic. At one year of age, an incomplete resection of an extradural tumor extending from D12 to L2 was performed. Three varieties of neurogenic tumor, ganglioneuroma, neuroblastoma and neurofibroma, were found in different sections of the tissue removed.

Fig. 2. Male, aged five, with an inoperable retroperitoneal neuroblastoma, was treated by irradiation. He survived three years and although he developed no metastases, he succumbed as a result of hemorrhage within the tumor.

Knox and Pillers[2] appraised the future of 14 surviving patients out of 126 with neuroblastoma by utilizing the method described by Collins *et al.*[1] in estimating the prognosis of Wilms's tumors. They found that these 14 children with neuroblastoma had lived beyond the "period of risk" and so could be considered to have a favorable prognosis. The validity of the concept in the case of neuroblastoma may be questioned since

Fig. 3. (*A*) Female, aged sixteen months, who nine months previously was found to have an inoperable neuroblastoma of the left adrenal gland and a neuroblastoma in the liver. She was treated with radiation, nitrogen mustard, methotrexate and radioactive phosphorus. Emaciation, ecchymoses about the orbits and chemosis of conjunctivae are evident. (*B*) Same patient at the age of nine. She has left amblyopia and reduced hearing. Not visible here is a basal cell carcinoma of her left cheek.

the variability in its growth potential at different age periods of the host has yet to be determined. Figure 4 shows a boy in whom several of the multiple cutaneous and subcutaneous masses which developed in 1936 at the age of four months were treated by irradiation. They all disappeared. A retroperitoneal ganglioneuroblastoma and a ganglioneuroma of the thoracic wall did not become clinically manifest until the boy was eighteen years of age. It is possible that this child's disease could have been of multicentric origin and that the different sites had different growth potentials.

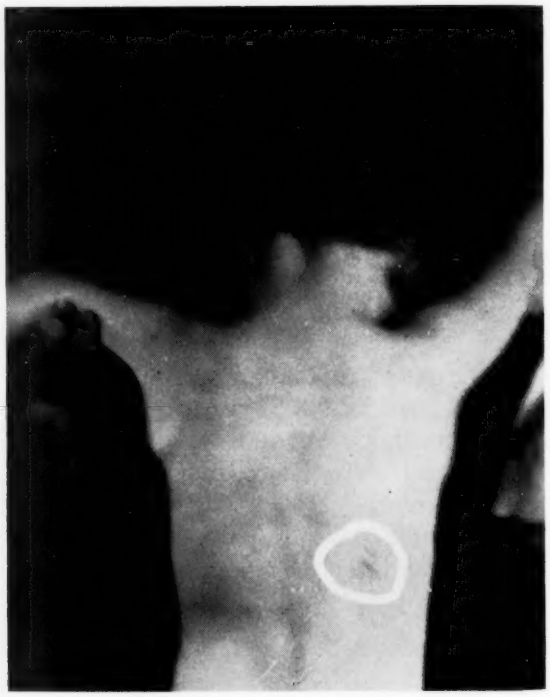

Fig. 4. Male, aged one, who had multiple subcutaneous nodules noted initially at four months of age. One lesion is encircled in the illustration. Biopsy of two of the tumors showed neuroblastoma. A roentgenogram of the abdomen showed no soft tissue or calcified mass. Coley's toxins were administered. Three lesions were irradiated and all, including those not treated, regressed. At the age of twenty Dr. Robert R. Smith operated on him at the Clinical Center of the National Institutes of Health, and removed a retroperitoneal ganglioneuroblastoma and a ganglioneuroma of the right thoracic wall.

SUMMARY

It seems evident that the natural history of neuroblastoma may vary greatly from

child to child. Surgery and irradiation are the recognized therapeutic modalities. Chemotherapy is still of questionable value but investigation of its effects should be continued.

The prognostic evaluation must be guarded, for as in other cancers, the five year, ten year or longer survival "yardsticks" may prove erroneous in some instances.

Memorial Center for Cancer
and Allied Diseases
444 East 68th Street
New York 21, New York

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ROENTGEN THERAPY OF SKIN AND LIP CARCINOMA: FACTORS INFLUENCING SUCCESS AND FAILURE*

By CARL F. VON ESSEN, M.D.
NEW HAVEN, CONNECTICUT

THE results obtained in the treatment of carcinoma of the skin or mucosa of the lip are, in general, good and cure rates following radiation therapy or surgery approach 100 per cent for early lesions. There appears, however, to be some difference of opinion concerning the optimum radiation dosage in different stages of disease. The grave consequences of initial failure of treatment are well known and, therefore, irradiation of a curable neoplasm is generally carried to what is judged to be the limit of tolerance of normal neighboring structures. Such doses, when successful in eradicating the tumor, may be higher than necessary to obtain a high probability of permanent tumor regression. The expected cosmetic sequelae of treatment of curable carcinoma of the skin and lip are important in the consideration of the choice and degree of treatment. A more precise estimation of optimum dosage may depend upon numerous variables, some of which will be considered here.

CRITERIA OF ANALYSIS

The carcinomas of the skin and lip in this report form a diverse group of lesions with respect to size, histology, and treatment history, arising in different locations in various individuals. Valid criticisms have been made concerning analysis of such heterogeneous populations of tumors.[6] With sufficiently large numbers, it may be possible to study the influence of individual characteristics upon the response to irradiation by separation of lesions into categories. An attempt to accomplish this aim is made by studying the relationships of the following factors to treatment results.

BIOLOGIC FACTORS

1. *Tumor and Surface Area.* Accurate tumor measurements were not available on all lesions. The exact dimensions of the field of irradiation are recorded, however, and its area serves simultaneously as a useful index of the tumor area and a more accurate measure of effectively irradiated tissue area which includes normal epithelial margin and tumor.

2. *Histology.* A microscopic diagnosis of either basal cell carcinoma, basosquamous cell carcinoma or squamous cell carcinoma was made in all lesions. No lesions considered premalignant or noninvasive are included.

3. *Location.* The lesions are classified by the following sites of origin: nose, eyelid, ear, lip, trunk and extremities, and face (comprising the remaining sites of the head, including the scalp and upper neck).

4. *Previous Treatment.* Included in the material are the lesions with a history of previous unsuccessful treatment. The majority of these treatments consisted of electro-desiccation. The range of other types of interference included nitric acid cautery, caustic paste applications, local corrosive injections, and curettage. A minority of lesions were recurrent following surgical excision, radium and roentgen therapy.

Data on other tumor and host characteristics such as growth rate, gross morphology, and skin condition were not uniformly available and, therefore, could not be subjected to analysis. The age of the patient may have a bearing upon the response to treatment. The great majority of

* From the Tumor Institute of the Swedish Hospital, Seattle, Washington. This study was made while the author was a trainee of the National Cancer Institute.
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TABLE I

DISPOSITION OF PATIENTS WITH DIAGNOSIS OF MALIGNANT EPITHELIOMA OF THE SKIN OR MUCOSA OF THE LIP SEEN AT THE TUMOR INSTITUTE OF THE SWEDISH HOSPITAL, 1938–1955

Tumor Location	No. of Lesions							
			Roentgen Therapy					
			Followed					
				Under 3 yr.				
	Surgical Excision	Radium	Over 3 yr.	Lost	Died of Intercurrent Disease	Not Biopsied	Consultation: Not Treated	Total
Face	187	23	222	50	27	55	44	608
Eyelid	34	2	78	14	9	6	4	147
Nose	54	4	107	37	5	25	16	248
Ear	37	0	16	6	2	2	2	65
Lip	31	7	131	21	8	10	12	220
Trunk and Extremities	33	4	11	7	4	0	8	67
Totals	376	40	565	135	55	98	86	1,355

patients were between the ages of fifty and seventy, and by superficial examination of the data it was felt that it would be impossible to ascertain whether age influenced the therapeutic results. This was, in part, because of the higher rate of intercurrent deaths and loss of follow-up examinations in the older patients.

PHYSICAL FACTORS

Nearly all lesions were treated with equal fractions of roentgen radiation at daily intervals, excepting Sundays and occasionally Saturdays. The cumulative time period of this treatment scheme ranged from a fraction of one day (single treatment) to six weeks.

Roentgen rays generated at 120–140 kv. peak were used in the treatment of 87.5 per cent of the lesions. In most instances, the half value layer was 2 mm. Al, and the focal skin distance, 15 to 30 cm. Ten per cent of the lesions were treated with 200–250 kv. peak roentgen rays (1.5 to 2 mm. Cu half value layer). Fifteen cases, or 2.5 per cent, were treated with 800 kv. peak roentgen rays (half value layer of 3 mm. Pb). In the great majority of superficial and small carcinomas no corrections for depth were computed; stated doses are equivalent to surface exposure doses with full backscatter. In the more advanced and thicker lesions, the depth of a lesion was estimated and a minimum tumor exposure dose was calculated. All equipment was calibrated by means of National Bureau of Standards corrected Victoreen condenser r-meter measurements. In the case of 800 kv. peak radiation, the thickness of the thimble chamber wall was increased sufficiently to produce electron equilibrium within the air cavity. Analysis of the present data was done entirely in units of exposure dose—*i.e.*, without corrections appropriate either to absorbed dose or relative biologic effectiveness. Exposure dose rates varied from about 20 to 300 r per minute.

DESCRIPTION OF CLINICAL MATERIAL

The records of over 1,100 patients bearing a total of 1,355 epitheliomas of the skin and mucosa of the lip were studied (Table 1). These patients were initially seen be-

TABLE II

INCIDENCE OF LESIONS AND TREATMENT RESULTS RELATED TO FIELD SIZE AND LOCATION

Field Size in sq. cm.	Tumor Location																					
	Face			Eyelid			Nose			Ear			Lip			Trunk			Total		
	No.	R	N	No.	R	N	No.	R	N	No.	R	N	No.	R	N	No.	R	N	No.	R	N
<2	44	4	2	43	3	1	59	5	1	2	0	0	9	0	1	2	0	0	159	12 (8%)	5 (3%)
2 to 4	73	1	2	24	3	2	27	0	1	4	0	0	44	1	4	3	0	0	175	5 (3%)	9 (5%)
4 to 10	74	4	5	6	2	0	17	1	0	5	0	0	60	4	5	2	0	0	164	11 (7%)	10 (6%)
>10	31	8	2	5	0	0	4	1	0	5	3	0	18	3	2	4	2	1	67	17 (25%)	5 (7%)
Total	222	17 (8%)	11 (5%)	78	8 (10%)	3 (4%)	107	7 (6%)	2 (2%)	16	3 (19%)	0 (0)	131	8 (6%)	12 (9%)	11	2 (18%)	1 (9%)	565	45 (8%)	29 (5%)

No. = Total lesions.
R = Recurrences.
N = Necroses.

tween 1938 and 1955. Over 50 per cent of the lesions were treated by roentgen therapy. A smaller number were excised or treated by radium. Five hundred sixty-five tumors treated by roentgen therapy satisfied all of the criteria enumerated below and form the basis of the present analysis (Tables II–V). These criteria were:

1. Biopsy and microscopic diagnosis of invasive epithelioma. Several smaller lesions were excluded because the biopsy, as determined by study of the microscopic sections, may have removed the entire epithelioma. Lesions without biopsy were included only in the few cases where a proved recurrence or overdosage reaction developed.

2. Treatment by roentgen therapy.

3. A minimum of three years of follow-up examination: 292 lesions (52 per cent) were followed for at least five years; 49 lesions (8.7 per cent) were followed and observed for at least ten years. It was found that 38 out of the 45 recurrences (85 per cent) developed within the first three years following treatment, but that only 14 of the 29 necroses (48 per cent) appeared in this period. The apparent peak for development of skin necrosis was in the fourth year following treatment, while the peak for recurrence was in the first year. It would seem that the adequacy of this minimum follow-up period was more limited in detecting overdosage reactions than in detecting recurrent neoplasms.

CRITERIA OF RESULTS

Success of treatment is here defined as a minimum period of observation of a lesion showing satisfactory healing without evidence either of persistent or recurrent neoplasm, or of damage to normal integument resulting in ulceration, either temporary or permanent. It must be emphasized that, in this study, the criterion of *local* cure is used. Of some interest is the evaluation of damage produced by radiation that may eventually lead to *de novo* cancer in the treated area. Only 2 cases, not included in this series, represent possible instances of new tumor arising in the treated area following

TABLE III

RELATIONSHIP OF TREATMENT RESULTS TO RADIATION ENERGY AND FIELD SIZE

Energy of Roentgen Radiation	Size of Radiation Field												Total		
	0–2 cm.²			2–4 cm.²			4–10 cm.²			over 10 cm.²					
	No.	R	N	No.	R	N	No.	R	N	No.	R	N	No.	R	N
120–140 kv.	159	12	5	174	5	9	144	8	9	17	2	1	494	27 (5%)	24 (5%)
200–250 kv.				1	0	0	20	3	1	35	8	1	56	11 (20%)	2 (4%)
800 kv.										15	7	3	15	7 (47%)	3 (20%)
													565	45	29

No. = Total lesions.
R = Recurrences.
N = Necroses.

apparently successful radiation therapy. These are briefly reported.

REPORT OF CASES

CASE I. A squamous cell carcinoma arising in the right external auditory canal and helix, measuring 4×2×0.5 cm., was treated in 1946 with a 36 cm.² field of 800 kv. peak radiation to a dose of 6,050 r in thirty-four days. Satisfactory regression of tumor occurred and the patient was followed for ten years with only moderate atrophy of the skin of the auricle present. She was seen in 1956, with a friable, bleeding lesion appearing in the original tumor site. A biopsy was not obtained. Shortly thereafter, the patient had an accidental death.

CASE II. A basal cell carcinoma arising in the inner canthus of the lower eyelid was treated by a 4 cm. diameter beam of 200 kv. roentgen radiation to a dose of 4,200 r in twenty-three days in 1943. Satisfactory regression occurred and the patient was apparently free of disease until 1956, when a new epithelioma was noted within the area of moderate skin atrophy, but arising on the side of the nose distinctly removed from the original tumor site. This tumor was excised and proved to be a basal cell carcinoma.

Comment. Although the first patient had evidence of a tumor arising in the original tumor location, no biopsy was obtained. The origin of tumor in the second case was in a new site, but within the irradiated area.

TABLE IV

RELATIONSHIP OF HISTOLOGIC DIAGNOSIS TO TUMOR LOCATION AND INCIDENCE OF RECURRENCE

Location	No. of Lesions	Recurrences	Basal Cell Carcinoma		Basosquamous Cell Carcinoma		Squamous Cell Carcinoma	
			No.	R	No.	R	No.	R
Face	222	17	138	12	46	2	38	3
Eyelid	78	8	55	6	10	0	13	2
Nose	107	7	70	5	19	0	18	2
Ear	16	3	5	0	2	1	9	2
Lip	131	8	—	—	—	—	131	8
Trunk and Extremities	11	2	4	2	2	0	5	0
	565	45	272 (48%)	25 (9%)	79 (14%)	3 (4%)	214 (38%)	17 (8%)

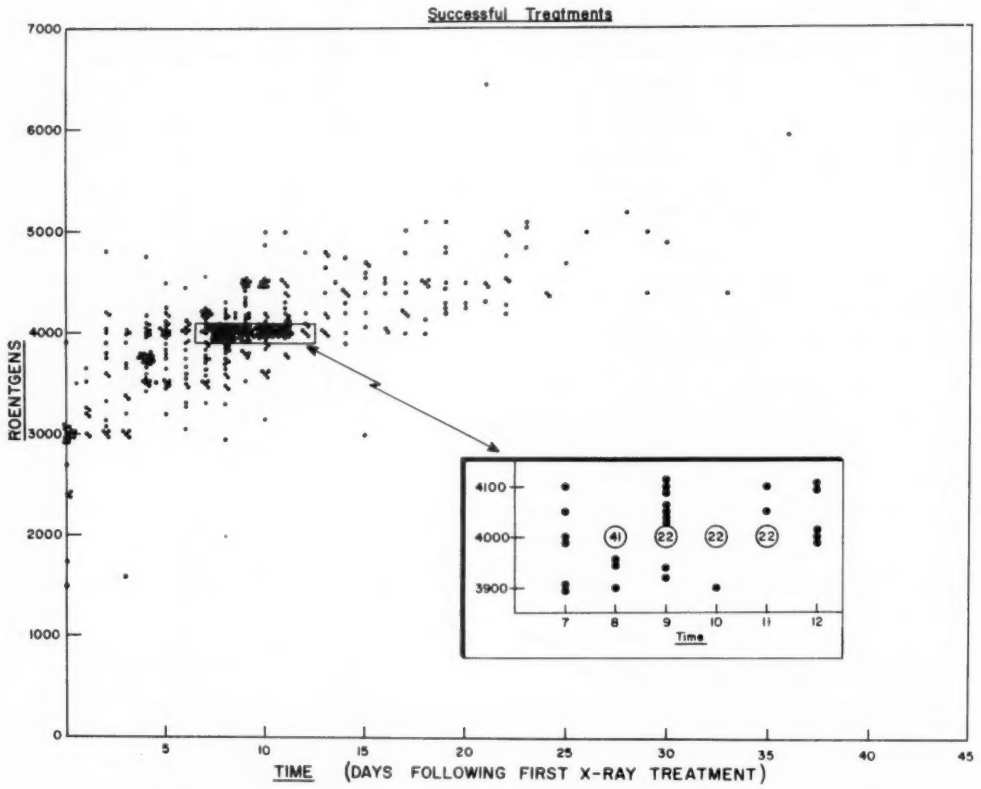

Fig. 1. The results of treatment: 491 lesions not developing necrosis or recurrence.

Treatment Results

For visual convenience, the over-all results obtained in the 565 lesions (Table II) are depicted in two similar scatter diagrams. The first diagram (Fig. 1) shows the group of successful treatments, each of the 491 points representing one lesion that remained healed throughout the observation period. The ordinate denotes the accumulated tumor dose in roentgens. The abscissa denotes the elapsed time in days following the first treatment with day zero indicating the time of the first treatment. The second diagram (Fig. 2) presents the distribution of (A) 45 recurrent lesions (shown as circles) and (B) 29 necroses (shown as crosses).

A. Recurrent Lesions

A total of 45 lesions persisted or recurred, giving a recurrence rate of 8 per cent. In Table II the rates of recurrence are com-

Table V

Results of Retreatment; Marginal Recurrences; Relationship to Field Area

Field Area	Total Lesions		Marginal Recurrences	Net Retreated Lesions			Net Initially Treated Lesions		
	No.	R	No.	No.	R	%R	No.	R	%R
0–2 cm.²	159	12	2	12	2	16.6	145	8	5.5
2–4 cm.²	175	5	1	19	1	5.3	155	3	1.9
4–10 cm.²	164	11	2	18	3	16.6	144	6	4.2
>10 cm.²	67	17	1	18	9	50.0	48	7	14.6
	565	45	6	67	15	22	492	24	5

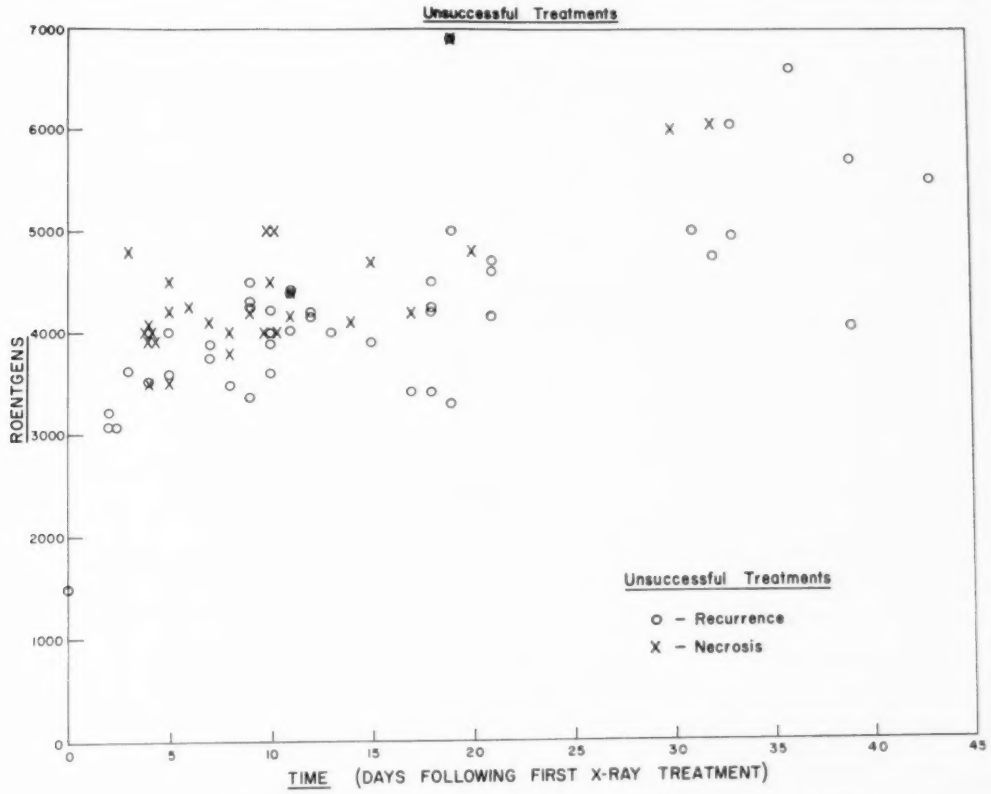

Fig. 2. The results of treatment: 45 recurrent lesions and 29 necroses.

pared for different tumor locations and areas of treatment field. There are no significant differences between lesions arising in different sites. Excluding the small number of ear and trunk lesions, the rates varied from 6 per cent in 131 lip lesions to 10 per cent in 78 eyelid lesions. There is a significantly higher recurrence rate (25 per cent) in 67 lesions that were treated with fields greater than 10 cm.^{2} when compared to the rest of the material (6 per cent, $\chi^2=28$; $P<0.01$). This decrease of local curability with increasing tumor size is well-known and has been noted by other investigators in the radiation therapy of cancer of the skin and lip[11,12] as well as in experimental tumors[13] and has also been studied as a general principle of radiation therapy.[7] The recurrence rates of lesions treated with fields smaller than 10 cm.^{2} did not appear to differ significantly, although the rates varied from 3 to 8 per cent among the three field size groups ($\chi^2=2.8$; $0.1>P>0.05$). The relationship of tumor size and radiation energy to treatment results (Table III) demonstrates the use of higher energies for treatment of the larger, poorly curable lesions. The highest recurrence rate (7 out of 15 lesions—47 per cent) is found in the group of lesions treated with 800 kv. peak roentgen rays.

The radiation energy selected, as shown, is largely determined by the independent variable of tumor size. Dosage is therefore compared among the categories of lesions treated by the three separate energy ranges. Because a majority of the lesions (87 per cent) were treated with superficial radiation, these are further subdivided into three field size categories. In each of the five categories so obtained, the mean accumulated dose and mean elapsed time and their standard deviations are plotted on linear coordinates for recurrences and necroses (Fig. 3). A relationship between increasing radiation energy, elapsed time and accumulated dose may be noted. By association then, the rate of recurrence

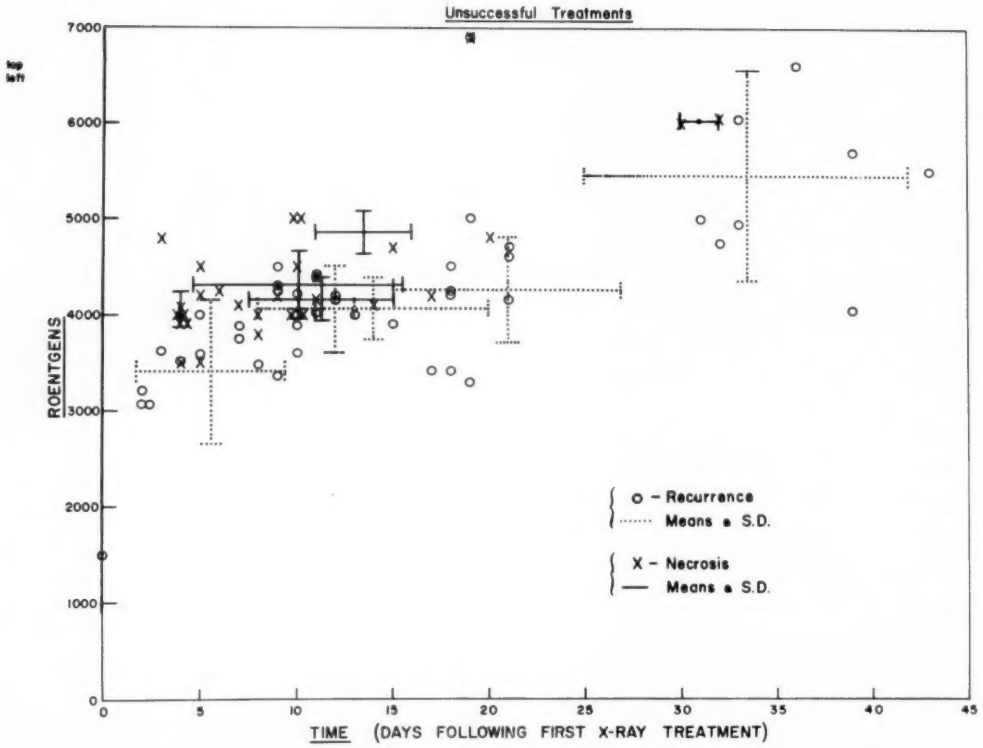

Fig. 3. Distribution of radiation energy for recurrences and necroses. From left to right the means and standard deviations of accumulated dose and elapsed time refer to: (a) 120–140 kv., 0–2 cm.² fields; (b) 120–140 kv., 2–4 cm.² fields; (c) 120–140 kv., fields greater than 4 cm.²; (d) 200–250 kv.; (e) 800 kv.

varies with tumor size and treatment energy as well as treatment time and dose (Fig. 4). Curability decreased with increasing tumor size and increasing radiation energy, and with increasing over-all treatment time and tumor dose. It may be remarked that the form of treatment was dictated by the extent of the disease, and the treated lesions progressively distributed along the time and dose axes of the scatter diagram are not comparable in respect to radiation curability.

There was no significant difference in the curability of basal cell carcinoma, basosquamous cell carcinoma and squamous cell carcinoma (Table iv). All carcinomas arising in the mucosa of the lip were squamous cell in type. To determine if any bias in the type of treatment may have masked true differences in radiation curability, the means and standard deviations of the dose and time components of the treated lesions were determined. The mean treatment time for the squamous cell lesions was 12.5 ± 6.7 days; for basal and basosquamous cell lesions, 9.4 ± 4.9 days. The accumulated mean doses were 4,070 ± 950 r and 3,860 ± 640 r, respectively. It appears that squamous cell carcinoma was, in general, treated slightly longer and to a slightly higher accumulated dose. The differences of dosage are small and not statistically significant and it is likely that any real differences in radiation curability are of small magnitude in this material.

1. *Marginal Recurrences.*

Eradication of localized tumors by surgery or irradiation is dependent upon treatment with adequate margins about the tumor. When treatment fails to incorporate all tumor tissue, persistence and progressive growth occurs. Epitheliomas of the skin and mucosa of the lip often arise in hyperkeratotic regions where microscopic nests of invasive carcinoma may occur. Six of the 45 recurrences were de-

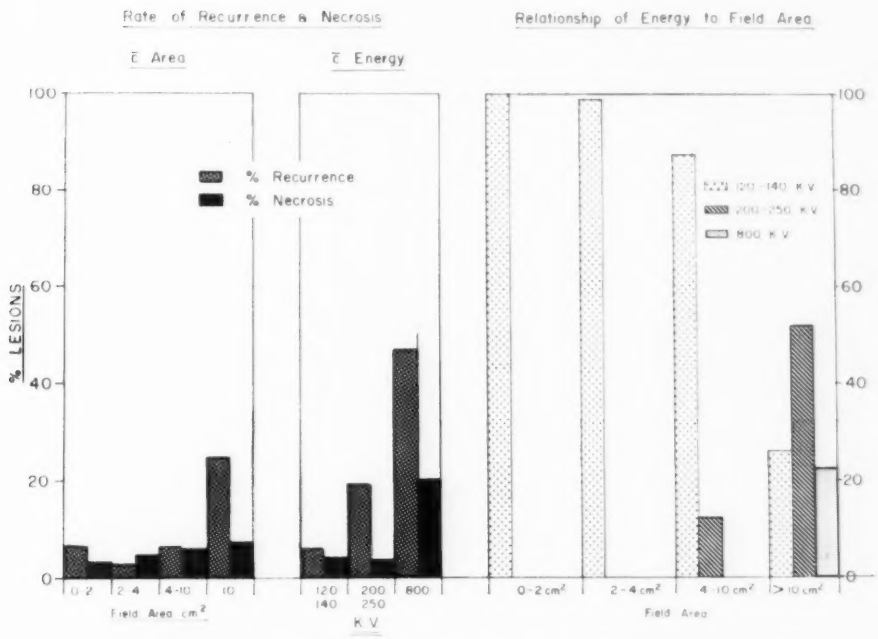

Fig. 4. The relationships of field area and radiation energy to results.

scribed as definitely arising outside of the margin of radiation reaction. A typical example is shown in Figure 5. In the analysis of the effect of dosage upon curability, it is apparent that recurrences ascribed to geometric misses of tumor cells have no necessary relationship to dose. It is possible that unirradiated marginal tumor would eventually grow into the irradiated area and mask the recurrence of central persistent tumor. This was not observed, however, because the marginal recurrences were promptly excised, and the original irradiated field remained free of disease.

II. *Recurrences Following Previous Treatment.*

Sixty-seven (12 per cent) had previous treatment, with subsequent persistence or recurrence of tumor. These were treated with roentgen therapy and 15 proved again to be treatment failures (22 per cent recurrence rate) by evidence of persistence and progressive growth. Over one-half of the re-treatment recurrences were far advanced infiltrating tumors of the face—still too

Fig. 5. (*A*) Squamous cell carcinoma of the right malar region. (*B*) Development of recurrence at the superior margin of the lesion treated by roentgen radiation. The recurrence is ascribed to geographic miss and is listed as a marginal recurrence.

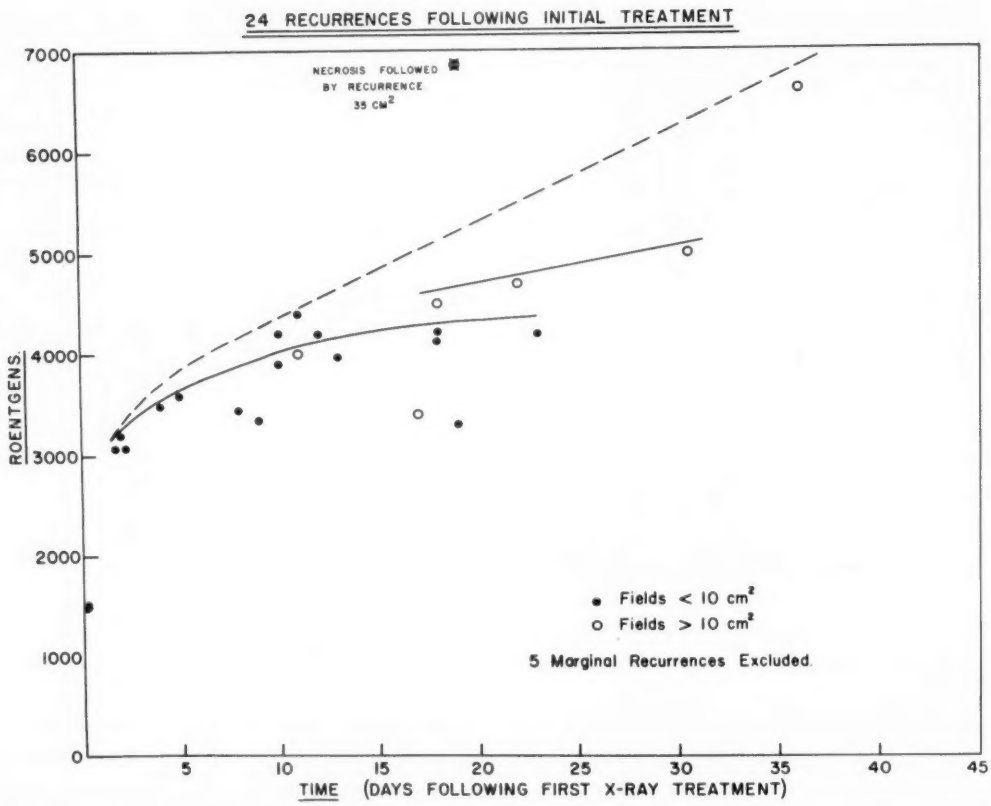

Fig. 6. Recurrent lesions following initial treatment. The lower curve is drawn freehand above the majority of small recurrent lesions. The middle curve is drawn above the majority of large lesions. The dashed curve is drawn above all lesions regardless of size, but excludes one supralethal point (at the top).

frequently encountered in clinical practice.

Table v summarizes the distribution of re-treated lesions and marginal recurrences as related to radiation field size. It appears that previously treated lesions form a class distinctly different from previously untreated tumors. Excluding the six marginal recurrences, the recurrence rates are 22 per cent and 5 per cent, respectively. The difference is 17 per cent $\pm$ 5.1 per cent and is significant at $P < 0.05$.

III. *Dose-Time Relationship.*

Du Sault[5] emphasizes the pitfalls in establishing dose-time relationships. It is not valid to derive a single curve expressing iso-effectiveness of dose and time for a spectrum of tumors differing significantly in radiation curability. The task is further complicated by the unequal distribution of this material along the treatment time axis. An approach can be made to the problem by including as parameters the two factors considered to greatly affect radiation curability—tumor size and previous treatment. A simplified derivation of iso-effect curves by empirical fitting of smooth curves relating a certain probability of cure to the coordinates of dose and time is attempted. The effectiveness of the curves to separate cured and noncured lesions is tested by Chi-squared analysis.

(1) *Previously Untreated Lesions* (total no. = 498). Two smooth curves are drawn in Figure 6 relating the most significant separation of cured from noncured lesions for small tumors and large tumors. The dashed curve demarcates the upper level of all recurrences (excluding the one "supralethal" point) for this category.

For convenience of analysis, it was desirable to transform the curves to straight lines. It was found that relatively little

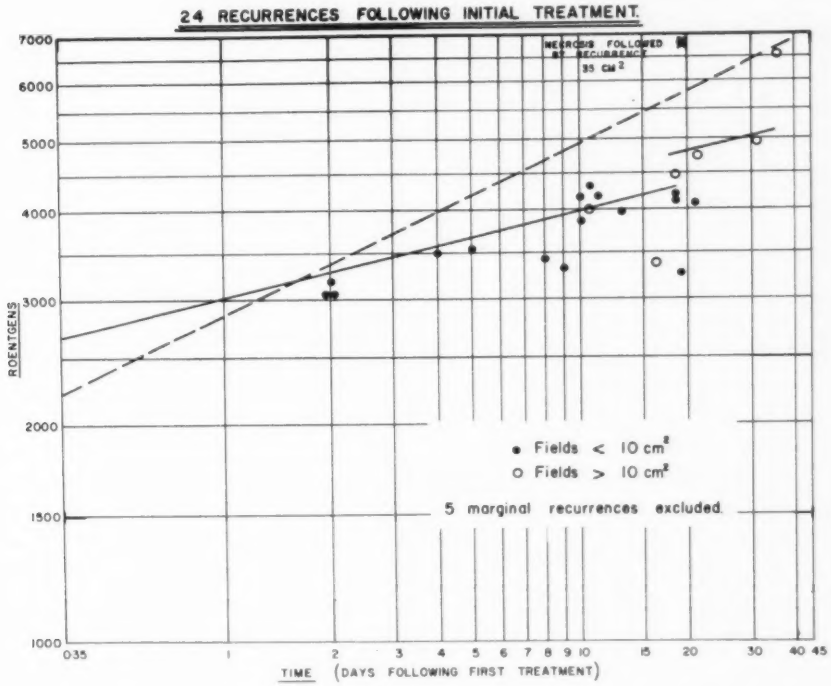

FIG. 7. Linear transformation of curves shown in Figure 6 to logarithmic coordinates on the scale proposed by Strandqvist.

distortion occurred by adopting a coordinate system proposed by Strandqvist[15] where the logarithmic values of the accumulated dose and of the elapsed time in days are used. The elapsed time of the first treatment was empirically placed, following fitting of Strandqvist's curves, to thirty-five hundredths of a day, approximately 8.4 hours following onset of treatment. Other authors[1,2] have used the logarithm of 1 for the first treatment and the logarithm of 2 for the treatment twenty-four hours later, etc. Figure 7 demonstrates this transformation. The logarithmic scale of the ordinate was made twice that of the abscissa for convenience of visual presentation.

(a) Small Tumors. The equation of the extended line expressing a 99 per cent probability of three year cure for the smaller lesions is $D = 2{,}680\ r \times T^{0.14}$ where D is the total dose in r and T is the treatment time in elapsed days. The total population of the small initially treated lesions is 444. The 17 recurrences represent 3.84 per cent. Of the cured lesions, 138 are found below the extrapolated line and 289 are above it. The recurrence rates for these two classes are 10.1 per cent and 1.04 per cent, respectively. A significant difference is present ($\chi^2 = 14.2$; $P < 0.01$). Empirical attempts at altering the χ^2 value by different slopes and intercepts of the line resulted in no further increase.

(b) Large Tumors. The line $D = 2{,}950\ r \times T^{0.14}$ shows no statistical significance as an iso-effect line separating the majority of recurrent large lesions from the cured large lesions. The lack of significance may be due to the small number of lesions. Fourteen cured lesions and one recurrence are present on, or above, the line (7 per cent recurrence), while 33 cured lesions are below the line with 5 recurrences (15 per cent recurrence) ($\chi^2 = 0.37$; $P > 0.5$). No empirical alterations of slope and intercept improved the value.

(c) "Absolute Cure" line. The significance of the dashed line $D = 2{,}300\ r \times T^{0.24}$, appearing to extend above all recurrent lesions in this category, is of a borderline nature. Fifty-five cured lesions are above

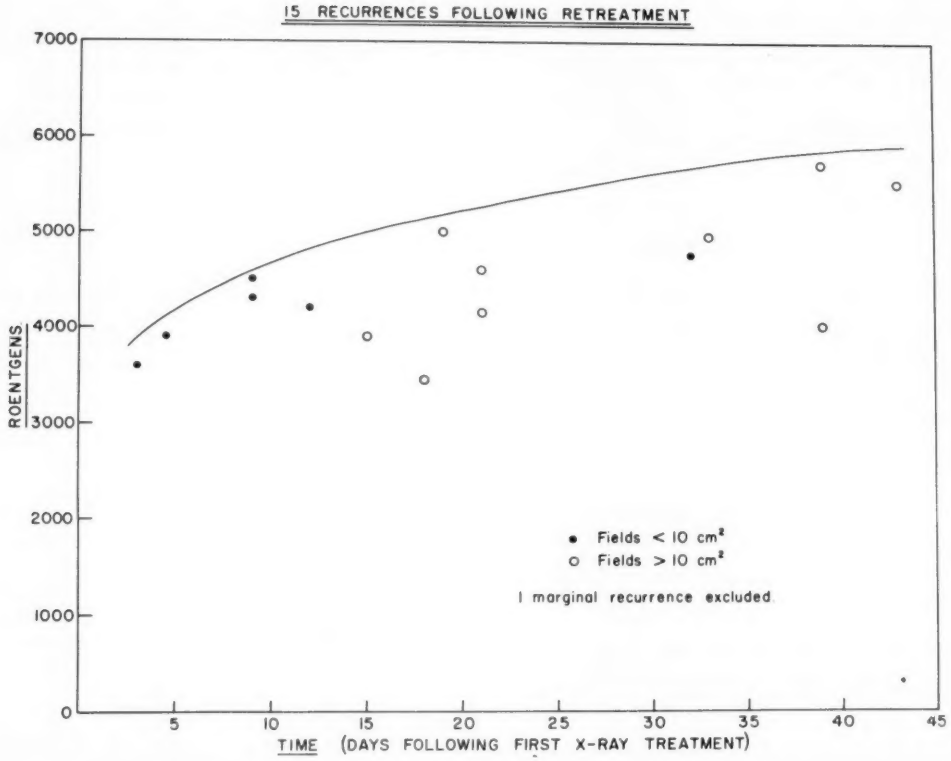

Fig. 8. Recurrent lesions following previous unsuccessful treatment. It is noted that a line drawn above these lesions extends above the great majority of all treatments. The line has, therefore, little validity.

the line with no recurrences and 420 cured lesions are below the line with 23 recurrences ($\chi^2 = 2.95$; $P > .05$). A single point at 6,900 r in 19 days represents a possible instance of "supralethal" effect and is excluded from the calculations. It is noted that this equation is close to the value proposed by Strandqvist to represent the optimum iso-effect line for cure of carcinoma of the skin; namely, $D = 2{,}250\ r \times T^{0.22}$.

(2) *Previously Treated Lesions* (total no. = 67). Figure 8 shows the 15 recurrences appearing among 67 previously treated lesions. A smooth line was again drawn above the recurrences and the significance of this line evaluated. Only 2 cured lesions are to be found above the line and, therefore, no statement of significance can be made referring to the minimum dosage yielding a high probability of cure for these lesions. It was not possible to make any statement of the significance of tumor size in this category.

B. NECROSES

Twenty-nine instances of necrosis appeared among the treated lesions (5 per cent). The great majority of the necrotic lesions eventually healed. One unusual case of a carcinoma of the lip was treated by means of 800 kv. roentgen rays to a tumor dose of 6,900 r in nineteen days and was followed by regression of the tumor and persistent, debilitating necrosis of the lip and mandible. Six years and four months following completion of treatment, a biopsy revealed the presence of recurrent neoplasm. This single instance suggests the validity of the "supralethal" dose suggested by Paterson.[14] This point lies far above the remaining data on the time-dose axis.

The factors which may have affected the rate of occurrence of necrosis were analyzed as follows:

Location. The rate of necrosis varied from 0 to 9 per cent in different sites (Table II). The only significantly different value

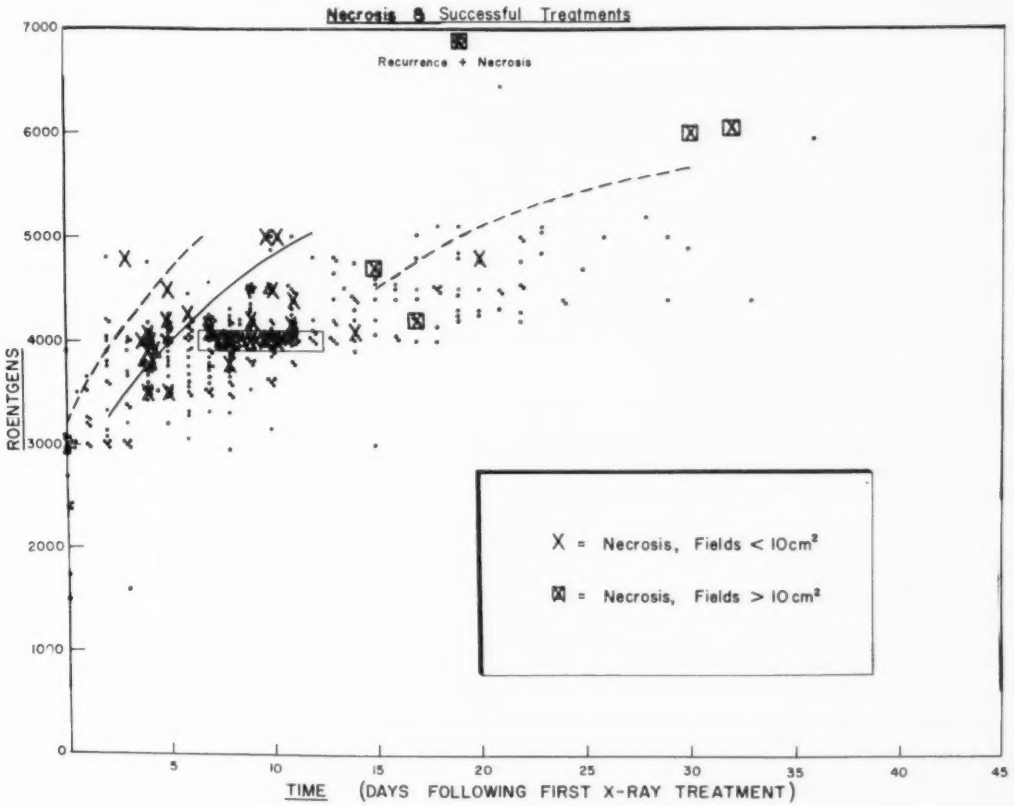

FIG. 9. Lesions developing necrosis. The freehand curves are drawn; they give a maximum statistically significant separation of successful treatments from necroses. From left to right the curves refer to: (a) fields less than 1.2 cm.²; (b) fields less than 10 cm.²; (c) fields greater than 10 cm.².

was the high rate in the lip (9 per cent, $\chi^2=4.6$; $P<.05$).

Field Size (Table III and Fig. 4). The values progressed from 3.14 per cent for fields less than 2 cm.² to 7.46 per cent for fields greater than 10 cm.². Greater differences may be masked by the different radiation energies used in the various field size categories, since the skin and mucosal effects are very dependent on quality of radiation.

Energy (Table III and Fig. 4). Of the 15 lesions treated with 800 kv. peak irradiation, 3 (20 per cent) developed necrosis (one of these eventually developed recurrent tumor, see above). A statistically significant difference, however, was not obtained because of the small numbers involved.

Previous Treatment. Of lesions that had received previous unsuccessful treatment, 2 developed necrosis. The difference in rate from the remainder of the material (3 per cent as against 5 per cent) is not significant.

Dose-Time Relationship. In the dose-time analysis of recurrences, the lesions were classified into groups treated with fields greater than 10 cm.² or less than 10 cm.². For purposes of comparison, the necroses are similarly classified and plotted in Figure 9. An attempt was made, for both of the field size categories, to delineate the slope and position of a line separating the majority of successfully treated lesions from the necroses.

(a) Small Fields. A number of slopes and intercepts appeared to give values of similar significance. The equations ranged from $D=2{,}500\ r\times T^{0.20}$ to $D=1{,}400\ r\times T^{0.34}$. The equation $D=1{,}950\ r\times T^{0.27}$ appeared to give the most significant separation for small fields ($\chi^2=21$; $P<.01$). This line separated 60 lesions above the line with 11 necroses (18 per cent) from 438 lesions

below the line with 13 necroses (3 per cent).

(b) Large Fields. The small number of large field necroses rendered it impossible to estimate a slope for the field size. If the slope is arbitrarily given the same value as that for the small lesions, then the equation of the line displaced to incorporate the large field necroses is $D=1{,}700\ r\times T^{0.27}$. The larger lesions above this line total 16 with 4 necroses (25 per cent), and below the line 51 with 1 necrosis (2 per cent) ($\chi^2=6.2$; $P<0.01$).

A cluster of 12 points representing successful treatments is found on the time-dose chart at the dose level of 3,000 r in one treatment (Fig. 1). The field sizes ranged from 0.78 cm.^{2} to 1.2 cm.^{2}. No late severe skin changes or necroses were noted in these fields, nor were any noted in fields of this minimum size at other dose-time coordinates. It would seem that the probability of necrosis in such small lesions is not likely at the dose levels reached in this material. Therefore, an iso-effect line yielding a low probability of necrosis for very small fields probably lies above the point, 3,000 r in one treatment.

DISCUSSION

Increase of tumor size appears to decrease radiation sensitivity as measured by the dose necessary to produce cure;[7] increase of irradiated normal epithelial area appears to increase its radiation sensitivity as measured by dose necessary to produce necrosis.[9,10] The basis of fractionation of radiation dosage rests upon the assumptions that tissues recover at different rates from the effects of irradiation and that tumor tissue, in general, recovers more slowly than nonmalignant tissue. The tendency to irradiate large tumors for longer periods of time has been demonstrated in this material and has been noted in other reports.[1,3,4,8,11,12,15] An example is seen in the report by Hale and Holmes[8] where two treatment schemes were used: a single treatment in 893 cases, and fractionation of dosage "within one week" in 113 cases. Optimum doses of 2,700 r for one treatment and 4,500 r for fractionation "within one week" were derived. The tendency to fractionate the larger lesions was stated although not quantitatively expressed, and therefore the two classes of lesions were not comparable in radiation sensitivity. It would not seem appropriate, then, to connect these two points of optimum dosage with an iso-effect curve. Such a curve relating equal probabilities of cure to both large and small lesions may only be applicable to particular tumor sizes over limited segments of the line. Attempts to shorten the fractionation schedule for a particular sized lesion in accordance with such a time-dose equation may result in a decreased probability of cure.

The iso-effect lines derived from the data in this report have limited validity because of the relatively small number of points used for scoring (45 recurrences and 29 necroses). The slopes for skin necrosis and tumor cure iso-effects appear to differ significantly when the initially treated lesions are studied in relation to field size. The slopes do not differ significantly when general analysis of the total material is made.

On the basis of the following assumptions, a model can be proposed:

1. The iso-effect lines for both late skin changes and cure of skin and lip carcinoma traverse simple parabolas on a linear time-dose coordinate system.

2. The iso-effect lines vary with area of irradiated skin and similarly, with tumor area.

3. The parabolas for each category, skin effect and tumor cure, form a family of curves, $D=k_sT^n$ and $D=k_tT^m$, respectively.

The data derived from this material suggest that the iso-effect line for 99 per cent probability of cure for the initial treatment of small tumors has a slope of 0.14 with an intercept at the single treatment axis of 2,680 r. If it is assumed that larger lesions have parallel iso-effect slopes with progressively higher intercepts at the single treatment axis, then a family of parabolas, transformed to lines on logarithmic coordinates, will have the general equation $D=kT^{0.14}$.

Similarly, a family of parabolas can be

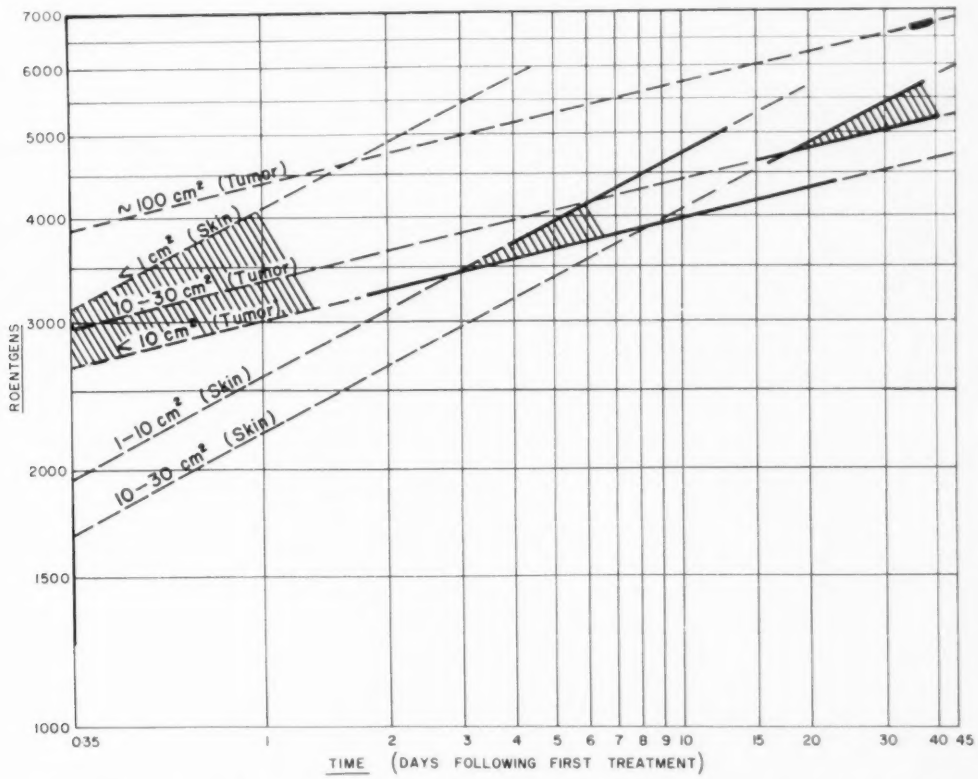

FIG. 10. A hypothetical model based on the derived curves with assumptions that k varies while m and n remain constant in the equations $D=k_{skin}T^n$ and $D=k_{tumor}T^m$. The shaded areas refer to favorable therapeutic regions for particular treatment situations. For example, a lesion treatable by a field of 8 cm.² may be treated with 3,450 r in 72 hours but may be more safely treated with a dose somewhat over 4,000 r in 240 hours.

developed for a certain probability of skin necrosis. In the data presented, a slope of 0.27 was derived for the line limiting the probability of skin necrosis to about 3 per cent for smaller radiation fields. If the iso-effect lines are parallel for different field sizes, then the family of parabolas will have the equation $D=kT^{0.27}$. Such parallelism has been suggested for skin tolerance and tumor cure from data derived from various sources by Du Sault.[5]

Superimposition of these two sets of parallel lines with different slopes illustrates the proposed model (Fig. 10). It must be emphasized that the material only yields sufficient data for treatment periods up to approximately three weeks. In addition, only two of the iso-effect lines have been derived directly from the data. The construction of all the other curves parallel to these two originally derived curves is, then, hypothetical. The principle of the model consists in predicting the therapeutic ratio for a particular treatment situation. The point at which two lines intersect marks the beginning of a progressively increasing area of favorable therapeutic ratio; *i.e.*, probability of cure/probability of damage, for a particular treatment situation to which the lines are appropriate. This possibility has been discussed by Andrews and Moody.[2]

The data suggest that use of a single value of radiosensitivity, k, in the equation $D=kT^n$ for carcinoma of the skin and lip, as advanced by Strandqvist, may not be valid for a spectrum of tumor sizes or for treatment fields of varying area. Previous treatment also appears to alter the radiosensitivity. The data do not determine whether the recovery exponent, n, changes with varying size or other factors.

SUMMARY

1. Five hundred and sixty-five histologically verified carcinomas of the skin and lip were treated with roentgen therapy and the results evaluated after observation periods of three to eighteen years.

2. In addition to dosage, the factors appearing to influence treatment results are tumor size and previous unsuccessful treatment.

3. The time-dose relationship is studied with reference to these factors.

4. A model is suggested incorporating the concepts of differential recovery of skin and tumor and differential radiosensitivity of tumor volumes and skin areas.

Department of Radiology
Yale University School of Medicine
789 Howard Avenue
New Haven 4, Connecticut

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PSYCHIATRIC PROBLEMS IN PATIENTS UNDERGOING RADIATION THERAPY*

By HOWARD HICKS ASHBURY, M.D.
STAUNTON, VIRGINIA

THE basic concept to be explored in this essay is that in radiation therapy (as in any form of therapeutics) it is essential to have a positive relationship between the patient and doctor, and that the quality of this relationship is an important factor in the end result.

Szasz and Hollender[5] have delineated three basic models of the doctor-patient relationship which they call (a) activity-passivity, (b) guidance-cooperation and (c) mutual participation. Activity-passivity indicates a state in which the patient is passive or inert. He or she does not actively contribute and may be unconscious, comatose, stuporous, terrified or otherwise unable to respond. The patient's body is available but beyond this there is no participation in the therapeutic process. Not only is the doctor the active party but he is in absolute control and the emphasis is upon the doctor doing something to the patient. Clinically, this model would apply to situations in which the radiotherapist inserts radium into the cervix or uterus of an anesthetized patient or implants radon tubes into the operative site of a radical neck dissection. The prototype of this situation would be that of a benevolent and omnipotent parent administering to a helpless infant who can neither help himself nor understand what is being done for him. In the patient's eyes the physician is no longer a person but the embodiment of skill, knowledge and understanding. It has been suggested[4] that this situation may gratify the needs of some doctors for mastery and contribute to their feelings of superiority. It is not unusual to hear surgical residents express a preference for the unconscious patient who arrives at the emergency room without friends, relatives or identity. Such a case is almost devoid of interpersonal relationships, explanations to families, need for operative permits, boring details, irrelevant history and other impedimenta which obstruct young Doctor Kildare in the swift completion of his miraculous, life-restoring science. I have been a surgical resident and I know.

I prefer to use the designation guidance-compliance rather than guidance-cooperation for our second model which postulates that the physician will tell the patient what to do and that the patient will obey. This patient who seeks out the physician for help is cast in the role of a student under a teacher, a child to a parent or an employee to an employer. The patient is expected to "look up to the doctor" and "to obey" him blindly and unswervingly. The doctor must be convinced that he is "right" and "knows what is best" for his patient. The doctor may enforce his orders by overt or covert threats, extraction of promises, authoritarian directives, etc., if he believes that what he demands is "for the patient's own good." This is a commonplace modality in general medicine and postoperative surgery. We see it most frequently in roentgen therapy when the patient comes for daily treatments. Here the radiotherapist may prescribe and dispense not only roentgen units but a schedule of activities, dietary advice, pharmaceutical aids, counsel on hygiene and emotional support. Carried to extremes this can degenerate into the so-called Pygmalion complex in which the physician loses sight of his patient as a human being and regards him as a potential statistic in a five year survival chart.

Mutual participation indicates a partnership in which the physician helps the patient to help himself. Such a relation is

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psychologically complex in that the participants are equally dependent upon each other. Not only does the patient need healing but the physician needs to heal the patient, and a successful resolution of the treatment situation brings mutual rewards to both. Friendship and identification are components of this interdependency. One of my colleagues, Bingham Dai,[1] has described a reciprocal relationship between persons in which one experiences the emotion of the other and also desires that the other shall share his own emotion. When he has communicated his emotion to the other, he attains a peculiar satisfaction that greatly enhances his pleasure and joy, or diminishes his pain. The prototype of this model is that of one adult to another or of an equal to an equal. Mutual participation is most often noted in psychotherapy, the management of diabetes and the treatment of many chronic diseases including the neoplastic ones. Unfortunately, this relationship is often inappropriate for the mentally deficient, senile, arteriosclerotic, illiterate or poorly educated person who lacks the potential to function as an adult. Some of our patients who survive must learn to live different lives, change occupations or work habits, and adjust to changing conditions. The woman who has undergone a radiologic menopause or received a lasting skin reaction may need more than hasty reassurance or tranquilizing pills to adapt to her body image. The patient with Hodgkin's disease, leukemia or recurrent metastases will have an indefinite need of palliative radiation therapy and a sound relationship with his doctor. These, and many others, are the people who need and profit from mutual participation.

The majority of patients coming to radiation therapy are beset by fear and anxiety. They must surrender their bodies to a procedure which may be both harmful as well as helpful. For many persons certain parts of the body and its functions are invested with intense emotion. The skin, face, head, breasts and reproductive organs are examples and great apprehension may be experienced when radiation therapy threatens to mar, disfigure or even destroy these structures. Sometimes the therapy entails additional pain or discomfort to the patient such as radiation sickness, loss of taste, dryness of the mouth, skin reactions and gastrointestinal disturbances. Added to these difficulties is the realistic possibility that death may be imminent. Our patients do not live in a vacuum immune to the thoughts, acts and emotions of those about them. The current public concern over the dangers of atomic energy and radiation; the recent daily progress reports in the press concerning the radiation therapy of a public figure; the false and destructive "reassurance" of uninformed persons; the gruesome recital of morbid histories by ghoulish "friends"; the influence of a neurotic family; the accumulated misinformation of the years; and similar environmental hazards beset the patient. Is it any wonder that we compare him to an infant, child or adolescent and structure his relationship to the therapist as one of passivity, compliance and obedience?

If our patients are beset by fears and anxieties, both obvious and concealed, it is only reasonable to adopt a liberal attitude toward the radiotherapists who have their problems also. Contrary to some reports, they are people, a heterogeneous group who possess individual personalities and have entered the field of medicine and radiology for motives of both a similar and dissimilar nature. Regardless, however, of any unique characteristics there are reality factors ever present which continually intrude upon the therapist's sense of well-being. He is an important person to his patient; he does carry great responsibility; and often his patient is dependent upon him for relief from pain and fear as well as for his very life and existence. This duty cannot be dismissed lightly. There is a discrepancy between what the patient expects and what the doctor can accomplish which is unavoidable in our present state of knowledge. I have described the problems of the radiologist as similar to those of the surgeon

intentionally. If a radiotherapist is aware of possible surgical complications as a part of his treatment; knows when it is justifiable to risk or produce these complications; and has the fortitude and ability to guide his patient through such a course with success; then, I believe we must accept him as one who possesses a high degree of competency.

I have set up three rather arbitrary types of response to these problems. The first type was described by Jones[2] in 1913 and he labeled it the "God complex." The symptoms are recognizable. Obvious vanity or conceit are less common than aloofness. The physician becomes relatively inaccessible; even the most trivial personal activity is placed in a "top secret drawer"; diction becomes circuitous, lengthy, involved and indefinite, and there is difficulty in cooperating with others. The physician becomes a man of mystery who encourages his patients to idolize him. Concurrently there is a disinclination to accept new knowledge because he already knows everything and cannot afford to admit mistakes. Jealousy of younger rivals and destructive criticism of colleagues soon appear. Pervading the entire situation is the need to help, protect and instruct the weak and the uninformed who acknowledge their helpless position and accept the role of a supplicant, "yes man" or member of the *claque*.

In contrast we have the philosophy of nihilism. The doctor feels that he has never cured anybody of anything, that the riddle of cancer will never be solved and that treatment is futile. An attitude of apathy arises. What difference does it make if the optimum depth dose is not obtained, if the cervical capsule is not exactly placed, or if the roentgen beam is inaccurately directed? Why attend meetings, read journals or seek instruction if the returns are unrewarding? Such a line of thinking can lead to retardation of thought and action, slowness of speech, hypochondriasis, feelings of guilt, and eventually to a major depression and hospitalization. The "God complex" and the nihilistic attitude may seem irrational but do not forget that they are meaningful. If treatment is unsuccessful and a patient is lost, the therapist can console himself on the one hand by saying, "If I couldn't cure him nobody could," and on the other hand by saying, "Nobody could have cured him so I am blameless."

I trust that the necessary brevity of my characterizations does not represent them as pure cultures or suggest a choice between Scylla and Charybdis. As a healthy third alternative we have the eclectic or "individualist."[3] Such a doctor is not only well trained but retains independence and originality in his thinking. He may not join or conform to any group but he is tolerant of the views and theories of others. Such an eclectic tends to narrow his field of specialization but retains interdisciplinary contacts through attendance at seminars and professional meetings. He is able to admit mistakes and evaluate accomplishments realistically. Emotional security is enhanced by cherishing democratic interpersonal relationships with all people—patients, friends, relations, colleagues, strangers and laymen.

CONCLUSION

I have presented the subject of patients, doctors and their relationships in a radiotherapeutic setting as I see it. If I have any conclusion to offer it is that there are no short, ready, general answers to the questions which have been raised. Flexibility or the ability to adjust to new situations is one of the characteristics of maturity. Certainly, the therapist who is aware of and can recognize the three models of relationship is in a better position to help his patient than he would be if he always functioned in a single mode. The doctor who treats cancer of the cervix and adjusts to activity-passivity (implantation of radium under anesthesia), guidance-compliance (daily roentgen therapy) and mutual participation (convalescence or recurrence) will seldom find his patients "uncooperative" or "difficult," and his patients will not leave him because he is "unsympathetic" or "doesn't understand my case."

In such a setting, questions such as "Should you tell a patient that he has cancer?" lose their meaning because they do not admit a definitive answer. Who are you addressing: an infant, a child, an adolescent or an adult, and what does the term "cancer" mean to that specific individual? We know that parents must constantly adjust to growing children. Are our patients any less deserving of our consideration? I hope I do not belabor the point too far if I make the platitudinous statement that our patients are human beings and that we should treat them as such.

In preparing this essay I have been more of an editor selecting ideas from the work of others, rather than a contributor of new, fresh or original thoughts. Men in every age have expressed these conceptions. In closing I will quote Francis Taliaferro Stribling, the first Superintendent of Western State Hospital. In a report to the General Assembly of Virginia on May 27, 1837, he stated his convictions regarding doctor-patient relationships and the psychiatric problems of his day . . . ; "we meet them as friends and brothers; we cultivate their affections; interest their feelings; arouse their attention, and excite their hopes; we cheer the desponding, soothe the irritated, and repress the gay; in a word we treat them as human beings, deserving of attention and care . . . "

SUMMARY

Any method of treatment (whether radiologic, surgical, medical, psychiatric, etc.) requires a variable degree of cooperation between the patient and physician. The type and quality of this cooperative relationship often determines the degree of success or failure. The factors affecting this proposition and its accompanying problems are considered specifically in relation to radiation therapy, and are discussed from a combined psychiatric and radiologic viewpoint. The author contends that the recognition and utilization of these factors is both indicated and rewarding.

Western State Hospital
Staunton, Virginia

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USEFUL ADDITIONS TO A SUPERFICIAL THERAPY MACHINE*

By JUSTIN J. STEIN, M.D.,† J. E. MORGAN, Ph.D.,† *and* C. L. CHALBERG‡
LOS ANGELES, CALIFORNIA

PROBABLY no single assemblage of roentgen-ray apparatus can ever incorporate every convenience desired by every user, so from a practical standpoint it has been found necessary to make certain refinements in our superficial therapy equipment. The additional features most desired were (1) the ability to set and maintain precise values of kilovoltage, and (2) to accurately and safely position the equipment when cones are used, particularly about the face. Suggestions as to how these refinements in technique can be accomplished are described in detail as follows.

1. ELECTRICAL

In earlier reports[1,2] one of the authors has already discussed the major advantages of providing continuously variable kilovoltage adjustment for all types of roentgen therapy equipment. Radiation output rates proportional to the second, or higher, power of potential emphasize the fact that kilovoltage settings are even more critical than tube current. Only by constantly maintaining exact values of both factors can the consistent delivery of accurately calibrated doses be expected.

The Picker type NR-2 control unit supplied for use with their Zephyr generator incorporates a ten-point minor selector switch with intervals of 3 to 4 kilovolts between adjacent steps. In order to effectively eliminate such gaps, it was decided to bridge across the entire unit with a continuously variable auto-transformer. For this purpose, a type W 10 M "Variac" (General Radio Company), which happened to be conveniently available, proved to have ample current carrying capacity to handle the relatively light load of the Zephyr high tension primary.

The schematic service diagram furnished with the NR-2 control identifies its kilovoltage selector switch points by letters D through P, each being connected to a correspondingly lettered tap on the autotransformer. For the sake of convenience, all these connections were left in place, and two additional leads were run from switch points D (minimum voltage) and P (maximum voltage) to the two ends of the Variac winding. The line leading to the main roentgen-ray exposure relay was then disconnected from the movable contact arm of the selector switch and changed over to the movable contact arm of the Variac. The Variac is now in parallel with the upper half of the autotransformer, and can supply, via the exposure relay, any portion of that voltage to the primary of the high tension transformer. In place of the original ten steps with average intervals ±10 per cent of the effective selector range, this 217 turn Variac reduces the unit of increment to 0.46 per cent, which is barely detectable on the panel meter. Readjustments may be made as desired, at any time during exposure.

In order to minimize the labor of installation, the encased Variac assembly was simply set on a shelf beside the control cabinet as shown in Figure 1. A section of 4 conductor no. 16 flexible cable provides the three current-carrying leads required, plus a ground connection to the metal box. With the cooperation of a Picker service representative who had a suitable scrap of cable in his tool kit, this entire project was completed in less than thirty minutes.

2. MECHANICAL

The relatively small size and light weight of the Zephyr tube head permitted the

* From the Department of Radiology† and the Research and Development Shop,‡ UCLA Medical Center, Los Angeles, California.

FIG. 1. Picker NR-2 control unit with Variac connected for continuous kilovoltage adjustment.

original design of its supporting stand to be quite simple. The basic mechanism consists essentially of friction controlled knuckle joints with adjustable tension clamps, pivoted from the top of a spring-counterbalanced vertical elevating column. Some

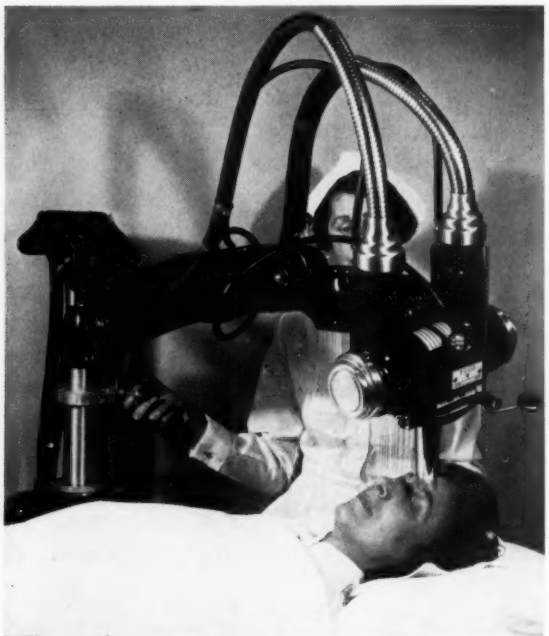

FIG. 2. Use of vernier adjustment to bring a sharp-edged cone into final contact with patient's face near the eye.

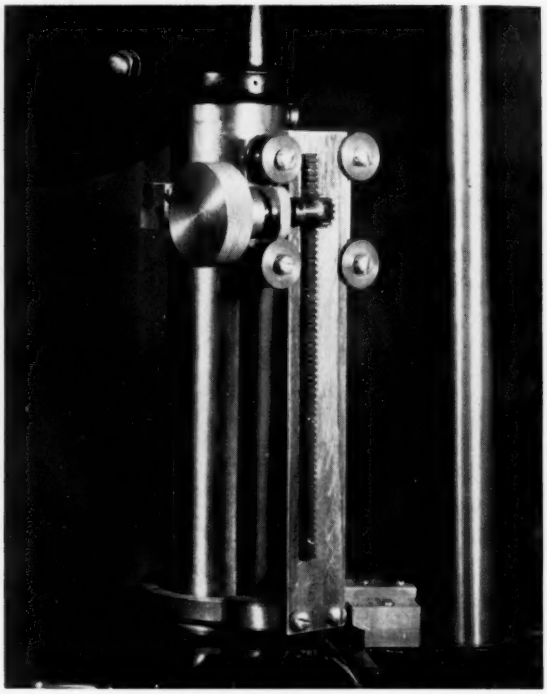

FIG. 3. Detailed view of rack-and-pinion geared vernier drive mechanism attached to elevating column of the Zephyr tube stand.

tendency toward backlash or over-riding of the desired position becomes apparent, however, when critical changes in elevation are attempted. The manufacturers of this machine formerly used, on their larger "220" model, a rack and pinion gear arrangement which provided much more satisfactory control of tube height. We have now applied a similar principle to the construction of an auxiliary attachment for the Zephyr stand. The action of this device permits up and down adjustment similar to that of the focusing device on a microscope, under complete control of the operator as seen in Figure 2.

The more detailed view of Figure 3 shows two sectional metal collars encircling the cylindrical elevating column. The lower collar, which fits loosely around this column and is bolted to the lower stand housing, supports a rigid vertical bar with a section of toothed track on its outer face. The upper collar is clamped securely to the

column, and attached to it is a carriage with four flanged guide rollers free to move up and down along the vertical bar as the support column telescopes within its housing. It will be noticed that the pinion gear mounted on this carriage and controlled by the large knurled hand wheel is shown meshed with its toothed track. In this position, rotation of the hand wheel moves the carriage and attached column through a vertical range of approximately $6\frac{1}{2}$ inches for fine adjustment. A pull on the hand wheel (toward the left of Figure 3) slides the gear drive out of engagement to allow preliminary rough positioning in the same manner as before the device was installed; then it may be pushed back into mesh for final vernier control. From these general ideas, illustrated by Figures 2 and 3, any good machinist should be able to construct a similarly workable device without serious difficulty and at a reasonable cost.

SUMMARY

Two accessory devices which have proved to be useful adjuncts to the Picker Zephyr superficial roentgen therapy machine are described: a continuously variable kilovoltage control and a precision vernier adjustment for elevating and lowering the tube head.

Justin J. Stein, M.D.
Department of Radiology
School of Medicine
University of California Medical Center
Los Angeles 24, California

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CONFIDENCE FACTORS IN THIMBLE CHAMBER DOSIMETRY*

By J. E. MORGAN, Ph.D.
LOS ANGELES, CALIFORNIA

IT IS now generally recognized that thimble chamber instruments used to calibrate radiation therapy equipment should themselves be recalibrated periodically by the National Bureau of Standards (NBS). When long distance transportation is involved, however, the danger that response characteristics may have suffered a significant disturbance during return shipment is not conducive to full confidence in the figures reported.

Although ±3 per cent tolerance limits are theoretically allowed in these NBS correction factors, past experience with large numbers of newly calibrated chambers used in that immediate vicinity and under rigidly controlled conditions[1] has shown the uniformity actually attained to be more nearly 1 per cent. On the other hand, a much less happy (but perhaps more prevalent) example was recently encountered in a large military hospital on the West Coast. There, three different r-meter electrometers with their respective chambers, all of fairly recent vintage and in apparently good condition, were found to disagree by as much as 19 per cent in response to the same roentgen-ray beam. Such contrasting situations present a strong argument in favor of some kind of constant reference source, capable of at least indicating whether or not the originally accurate instrument calibrations are still valid.

Having accepted the essentially unvarying gamma emission from sealed radium as a most logical standard of constancy, some practical minded investigators in this field have, from time to time, utilized various mechanical schemes to hold one or more radium needles in closely reproducible position with respect to an ionization chamber. By such means, once a basic calibration has been established, subsequent readings of apparent output from the radium permit quick detection and quantitative evaluation of any change in sensitivity of the measuring instrument. There is now also available a commercial product (Victoreen model 540) which offers some advantages over most of the previously improvised arrangements. In this device the radium is distributed in the form of a hollow tube, inside which certain of the more commonly used sizes of Victoreen chambers can be inserted. Concentric cylindrical geometry tends to obviate small distance errors, while an integral lead shielding container provides adequate protection to the user.

Being aware of the potential hazards to accuracy involved in commercial transportation of delicate instruments, the Radiological Equipment Section of the National Bureau of Standards has now agreed[2] to undertake a supplementary service. If a suitably shielded reference source as described above is submitted along with the radiation meter, a statement of apparent output (corrected to normal temperature and pressure) registered by the combination at the time of calibration may be requested in addition to the usual chamber correction factors. Thereafter, so long as similarly corrected check readings agree with those figures, the user is assured that no significant change in sensitivity has occurred. If a consistent discrepancy of moderate magnitude should appear, however, the numerical relation between original and current radium readings may be applied as an auxiliary correction, and the instrument may still be used with reasonable confidence.

In actual procedure, when a thimble

* Department of Radiology, University of California Medical Center, Los Angeles, California.

chamber is calibrated by NBS for a specified radiation quality, a scalar correction factor C is assigned which is valid for the specified atmospheric conditions of 760 mm. Hg and 22° C. Then so long as C remains constant the corrected value Dc of an observed dose Dx (measured at pressure Px and temperature Tx) may be found from the expression:

$$Dc = Dx \cdot C \cdot \frac{760}{Px} \cdot \frac{Tx+273}{22+273} \qquad (I)$$

Similarly, since the original NBS reference value Vs of apparent radium output was also normalized to 760 mm. and 22° C., any subsequent check reading Vx (observed at Px and Tx) must be changed to the corrected value:

$$Vxc = Vx \cdot \frac{760}{Px} \cdot \frac{Tx+273}{22+273} \qquad (II)$$

in order to permit direct comparison with Vs.

Now it is apparent that any disagreement between Vxc and Vs must be due to—and quantitatively equivalent to—a change in over-all sensitivity of the measuring device, which was stipulated by the original correction factor C in equation I. If we therefore multiply C by the additional factor or ratio Vs/Vxc, we have from I:

$$Dc = Dx \cdot C \cdot \frac{Vs}{Vxc} \cdot \frac{760}{Px} \cdot \frac{Tx+273}{22+273} \qquad (III)$$

Under the idealized condition of a perfectly stable instrument, Vxc would always remain equal to Vs, and equation III would be reduced to the original form of I. On the other hand, if we expand III by substituting the value of Vxc from II, we have:

$$Dc = Dx \cdot C \cdot \frac{Vs}{Vx} \cdot \frac{760}{Px} \cdot \frac{Tx+273}{22+273} \cdot \frac{Px}{760} \cdot \frac{22+273}{Tx+273}$$

and by cancellation:

$$Dc = Dx \cdot C \cdot \frac{Vs}{Vx} \qquad (IV)$$

This relation would appear to compensate indiscriminately for all forms of response variation, regardless of cause, and with no specific correction for ambient atmospheric density required.

Both the basic scale correction factor C and its corresponding radium standard reading Vs will have been predetermined for each chamber at the time of calibration. Any unknown dose reading Dx, together with a contemporary radium output check Vx, may then be substituted in equation IV to yield the final and fully corrected value Dc. It would seem, particularly in view of the fact that an accurate barometer is not always readily accessible, that this method may be actually more convenient to apply than the usual atmospheric correction formula quoted in equation I. It has been found in practice that one or two check values of Vx, taken shortly before and/or after the required dose measurements, yield satisfactory accuracy with very little extra effort. It should be noted, however, that the abbreviated form of equation IV offers no means for distinguishing between changes in Vx due to atmospheric conditions and those due to instrumental fallacies. It is therefore advocated that if this method is used, periodic additional checks be made using the Px and Tx corrections of equation II, in order to detect changing sensitivity or other anomalous behavior of the instrument itself. Any large or unstable discrepancy between Vxc and Vs will then serve as a warning that attention and repairs may be needed.

Since this is not essentially a new method but rather the tentative adoption of a relatively recent commercial product as a secondary reference standard, it is obvious that confidence in the results must rest principally on faith in constancy of the device. While no very long-term observations have been completed, two such sources have been employed during the past eighteen months for the procedures described above, including in each case a transcontinental round-trip via Railway Express. Check readings made before and

after each shipment, using Victoreen r-meters which remained at their respective home laboratories during the interludes, were found to agree within close limits of experimental error. Frequent "wipe tests" for radon have indicated no trace of leakage to date. The manufacturer describes the active element as a metallic foil, sealed between double stainless steel walls of the positioning cylinder. This construction should be less susceptible to packing or other forms of geometric shift than would be the case with a granular radium salt. Finally, since optimum exposures are of the order of five minutes or more, timing within significant limits of accuracy is not difficult.

It must be emphasized that these apparent values of radium output are to be considered as purely arbitrary scale units, useful only in determining reproducibility. Since there is no provision for electronic equilibrium, and the excessively short source distance prevents uniformity of ion density through the chamber volume, no interpretation in terms of roentgens should be attempted.

SUMMARY

A method is described which, by cross references to a suitably designed radium source, permits quantitative evaluation of sensitivity changes occurring in thimble chamber instruments at any time after their initial calibration. An abbreviated formula is derived to provide compensation for such changes, and at the same time to supplant, if so desired, the correction factors usually applied for ambient atmospheric conditions.

Department of Radiology
University of California Medical Center
Los Angeles 24, California

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A SENSITIVE GAMMA-RAY DOSIMETER*

By B. L. BLANKS, A.B., *and* R. H. ROHRER, Ph.D.
ATLANTA, GEORGIA

THE technique of measuring gamma-ray dose rate in phantoms and body cavities requires the use of a probe which does not appreciably disturb the radiation distribution. In this type probe,[1] a scintillating crystal is placed in the area in which the dose rate is to be measured. A light pipe transfers the luminescence from the crystal to a photomultiplier tube, the output current of which is proportional to the dose rate. Due to the relatively large physical size of the photomultiplier tube, it must be placed outside the primary radiation field in order to maintain normal equilibrium in this field.

Previous methods involve the use of a small, about 0.5 cc., anthracene crystal as the scintillator, a polished aluminum tube ($\frac{1}{4}$ inch diameter by 9 inches long) for the light pipe, and a 1P21 or 931A photomultiplier tube. The pulses from the photomultiplier tube are integrated and the resulting direct current measured with a DC microammeter. This system, used for cobalt 60 dose rate measurement, has a maximum sensitivity of about 1 r/hr. Since the photomultiplier tube is only 9 inches, or less, away from the primary radiation area, the current due to irradiation of the photomultiplier tube by scattered gamma-rays produces significant errors.

To improve the sensitivity of such a system, a $\frac{1}{4}$ inch diameter lucite rod may be used as a light pipe between the scintillator and the photomultiplier tube. This will increase the light collection by a factor of at least 10. However, lucite exhibits a weak fluorescence of its own. To remove this error, the light may be chopped at the junction of the scintillator and the light pipe.[2] Then, the peak-to-peak value of the alternating output of the photomultiplier tube will be proportional to the fluorescence of the scintillator alone. Note that this system also removes the error due to direct irradiation of the photomultiplier tube by scattered gamma rays.

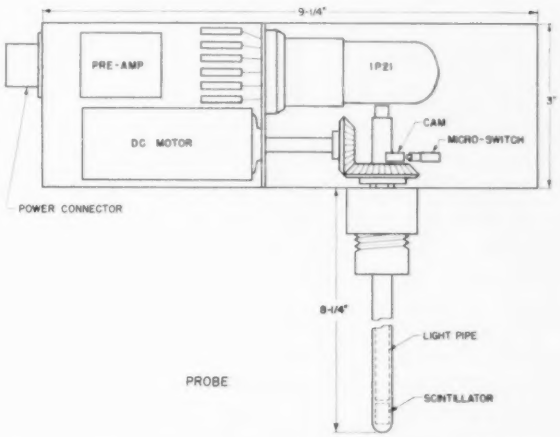

FIG. 1. The 6×12 mm. scintillator and the 6 mm. lucite light guide are contained in a thin-walled brass tube. The rotating mechanism, photomultiplier tube, and pre-amplifier are mounted in a $\frac{1}{32}$ inch steel case.

In the system described here (Fig. 1 and 2), chopping is accomplished by masking half the scintillator crystal face and half of the adjoining light pipe face, and causing the light pipe to rotate at 2 revolutions per second. This necessitates a small air gap at the junction between the light pipe and the scintillator which results in only a very slight reduction in the amount of light transferred.

The second detector must deliver a DC voltage proportional to the peak-to-peak value of the 2 cycles/second signal. A standard full wave rectifier would require an RC filter having a time constant in the order of ten seconds. This would be unsatisfactory, since it is necessary that the response of the output meter to sudden changes in dose rate be less than two seconds. This condition is necessary if the probe is to be used for field mapping or isodose curve plotting.

* From the Department of Radiology, Emory University, Atlanta, Georgia.
This work was sponsored by the United States Atomic Energy Commission.

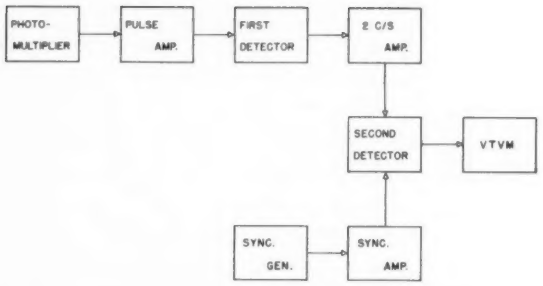

FIG. 2. Block diagram of complete system. The signal from the photomultiplier is in the form of one microsecond pulses, modulated at a rate of 2 cycles/second. This signal is amplified by the linear pulse amplifier. At the first detector, the pulses are integrated, leaving a 2 c/s sine wave, the peak-to-peak value of which represents the desired information. After passing through a range switch, the signal is amplified by a conventional low frequency amplifier before being detected.

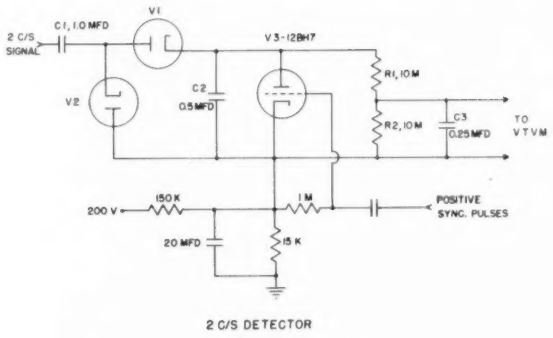

FIG. 3. A 2 cycles/second detector.

In Figure 3 is shown the circuit used to detect the 2 cycles/second signal. V_2 clamps the signal to the reference voltage at the cathode of V_3. The capacitor, C_2, is charged to the peak value of the signal by the diode, V_1. The RC time-constant across the plate of V_3 is long compared to the period of the signal. V_3 is normally biased to cut-off. The time response of the circuit is shortened by a one millisecond positive sync. pulse appearing on the grid of V_3. This pulse is synchronous with the 2 c/s signal, and is timed so that it reaches the grid of V_3 immediately before the crest of the following 2 c/s sine wave. This results in a short effective time constant so that for a 10 to 1 change in input, the output changes 99 per cent of this value in 1.5 seconds. Charging time for C_2 for a 1 to 10 increase in input level is 0.5 second. The discharge pulses are filtered by R_1 and C_3. The DC output voltage is measured with a vacuum tube voltmeter circuit.

The absolute dose rate sensitivity for an instrument of this type is determined by the statistical fluctuations in the output of the photomultiplier tube. The greatest *practical* sensitivity, while maintaining the fast response required, is limited by the number of photons absorbed by the small scintillator. The scintillator used here is a cylinder of anthracene, 6 mm. in diameter and 12 mm. long. Approximately 140 scintillations per second, or 35 scintillations per period in this case, are produced in a scintillator of this size when exposed to cobalt 60 radiation at 100 mr/hr. This results in a meter fluctuation of about ± 10 per cent at the 100 mr/hr. level, which is considered to be the maximum practical sensitivity for this instrument. In the absence of any radiation, the statistical fluctuation in the dark current of the photomultiplier tube produces a reading on the output meter corresponding to about 10 mr/hr.

Bruce L. Blanks
428 Woodruff Memorial Building
Department of Radiology
Emory University School of Medicine
Atlanta 22, Georgia

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EDITORIALS

RADIUM ACCIDENTS

"WHAT reason, like the careful ant, draws laboriously together, the wind of accident sometimes collects in a moment." This quotation from Schiller, the poet, may be considered pertinent in relation to the impetus imparted to the significance of radium accidents by the occurrence of certain recent events.

A newspaper account a few months ago described the delay of an urban renewal project in an eastern city due to the presence of a deserted building being razed in the area. This building once housed a clinic which later became radioactively contaminated in a fire. The radium in this case was one of the earliest and largest collections used in this country for obtaining radon. Most of it had been brought from Europe, but the interest it created engendered the development of the American radium industry for several decades to come.

Not long ago another unusual radium accident involving the spill of 25 mg. of radium in an operating theater was reported by Cross, Miller and Mussell.[1] Partial demolition of the hospital was necessary to decontaminate the building. In this instance the needle which ruptured was an old one of direct load type and the rupture was thought to be explosive, particularly in view of overheating of the radium container in sterilizing it.

Still another accident involving the spillage of 40 mg. of radium was reported in 1953 by Skow, Vandivert and Holden,[2] who described the decontamination procedures employed in removing radioactive material from the clothing, homes, automobiles and other surroundings of the involved persons.

A radium inhalation accident was reported in 1956 by Looney and Archer[3] in which two men were exposed following the rupture of a 50 mg. radium capsule. It has been noted that a discrepancy exists between the estimated amount of radium exposure and that retained by the body as evidenced by radon breath samples. Looney and Archer found that 76 per cent of inhaled radium was excreted in the first five days and that feces contained 97 per cent of the eliminated radium. Various methods of therapy were discussed by these authors.

In 1957, Gallaghar and Saenger[4] described the contamination of a hospital area due to the failure of a 50 mg. radium capsule which resulted in damages in excess of $250,000.

From these unusual events and others of a similar nature valuable lessons have been learned. Economically, accidents involving radium containers with contamination of surrounding areas can be most serious. Even more important, however, is the hazard to personnel. Exhaustive studies in this regard have been carried out by Gallaghar and Saenger,[4] and by Marinelli *et al.*[5] Of particular interest was the finding that the values resulting from single accidental

[1] Cross, F. H., Miller, H., and Mussell, L. E. Unusual radium accident. *Brit. J. Radiol.*, 1951, *24*, 122.

[2] Skow, R. K., Vandivert, V. V., and Holden, F. R. Hazard evaluation and control after spill of 40 mg. of radium. *Nucleonics*, 1953, *11*, No. 8, 45–47.

[3] Looney, W. B., and Archer, V. E. Radium inhalation accident—radium excretion study. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1956, *75*, 548–555.

[4] Gallaghar, R. G., and Saenger, E. L. Radium capsules and their associated hazards. Am. J. Roentgenol., Rad. Therapy & Nuclear Med., 1957, *77*, 511–523.

[5] Marinelli, L. D., Norris, W. P., Gustafson, P. F., and Speckman, T. W. Transport of radium sulfate from the lungs and its elimination from the human body following single accidental exposures. *Radiology*, 1953, *61*, 903–915.

exposure to radium sulfate dust varied considerably from previous values found in chronic radium poisoning in humans. These differences were primarily as follows: (1) The ratio of exhaled radon to total radium burden was distinctly lower, especially during the first six months; (2) the gamma-ray scanning pattern easily disclosed sharp localization of the element in the lung; (3) during the first year gamma-ray activity decreased in the lungs with an average half life of about 120 days; and (4) swallowed radium was eliminated early and apparently some of the material in the lungs was released and subsequently eliminated as well. The conclusion drawn is that estimates of radium body burden based on radon breath samples or excretion measurements alone are considerably in error in recent or acute single exposure to insoluble dusts. This work appears to have been later corroborated by that of Looney and Archer.[3]

Although the availability of artificial radioactive isotopes, *i.e.*, radiocobalt and similar radioactive elements, as radium and radon replacements, has decreased the absolute dependence upon radium, it is still believed that radium occupies a relatively unique place in intracavitary and interstitial therapy. A considerable number of radiologists and hospitals tend, therefore, to perpetuate its use, especially in the form of suitable applicators loaded with salts of the long-lived radium element itself.

To avoid the occurrence of radium accidents from such applicators, definitive important measures are necessary. It has long been known that an inherent tendency for radium containers to become more hazardous with age exists due to an increase in internal pressure. It has been emphasized that complete dehydration of the radium prior to loading of a capsule or needle is necessary to minimize the build-up of this pressure. Water decomposes into its component gases under the influence of irradiation, and, along with the alpha particle emission producing helium contributes to this pressure increase. Therefore, periodic checks of the competency of radium containers should be made. It has been recommended that this be done at least once yearly. The detection of faulty radium sources may be accomplished by visual evidence of the escape of a white powder from a container, or the direct observation of breakage. An indirect method of measurement would be to determine decrease in output. To detect subtle leakage, however, the utilization of a filter paper disk for demonstrating alpha activity, wipe tests for the same purpose or the sealing of a test tube containing the capsule to capture the escaped radon are other methods to be employed. Certainly, to detect a leak in a radium container as early as possible is of utmost importance to minimize contamination. A practical method for the detection of defects in radium needles and tubes and to demonstrate inequalities in the distribution of radium in these containers has been described by Freed, Pendergrass and Raufer,[6] who utilized an autoradiographic technique.

Measures to be taken following the recognition of such an accident include the control of personnel traffic in the area and the prevention of spread of contamination by air movement. In many of these reported incidents, unnecessary contamination of clothing, immediate surroundings, sidewalks, automobiles, and homes could have been prevented. An effective traffic control program also prevents recontamination during the clean-up procedure. An instinctive move to decontaminate the air in an immediate area may be to turn on the air conditioning system. Serious contamination of an entire building may result. Gallaghar and Saenger[4] have listed emergency measures to be taken following a radium accident which primarily entail sealing off the area as completely as possible. Decontamination with the use of appropriate clothing, vacuum cleaners, me-

[6] Freed, J. H., Pendergrass, E. P., and Raufer, H. Use of autoradiographs to detect defects in radium needles and tubes and inequalities in the distribution of the radium. *Radiology*, 1951, *56*, 99–103.

chanical and chemical removal methods can then be achieved. The disposal of contaminated articles in high level, moist solutions has been accomplished by sealing them in steel drums following which burial of the contaminated material was effected under the supervision of the Atomic Energy Commission. Other methods of disposal are also discussed. In order to avoid further dispersal of the low level residual contaminate, the area should be painted which has a favorable psychologic effect as well. Complete decontamination is usually impossible and some residual radium will remain as long as the building exists.

The problems posed by the presence of a radium contaminated building in an urban renewal area and the reports in past years of similar accidents occurring in hospitals or research laboratories where radium is being used serve to emphasize the need for adequate and periodic inspection of radium sources, in order that contamination with its attendant health hazards to personnel may be prevented. Simple methods of recognizing faulty radium containers can be employed by all who have radium sources. Defective tubes and needles must be reloaded. In addition to minimizing serious personnel exposure, unnecessary financial burdens may thus be avoided.

Kenneth L. Krabbenhoft, M.D.

Harper Hospital
Detroit 1, Michigan

SIMEON T. CANTRIL, M.D.

1908–1959

"Turn the problem as we may, the scientific side of irradiation belongs to the physicist. The application is still an art" (Cantril, 1940).

DR. SIMEON T. CANTRIL died on September 10, 1959 of coronary thrombosis. His loss is a crushing blow to American radiation therapy.

Cantril became interested in radiation therapy during his internship, under the influence of Dr. Max Cutler. Following his residency at the Tumor Clinic of the Michael Reese Hospital, the decisive, formative influence came in the years of his

association with Dr. Henry Coutard, first at the Institut Curie in Paris and then at the Chicago Tumor Institute. In 1938—at the age of thirty—he accepted the position as Director of the Tumor Institute of the Swedish Hospital in Seattle which he held until his death. In 1949 he was appointed Associate Professor of Radiology at the newly organized medical school of the University of Washington. During the war, he was drafted by the Manhattan Project, where—as an associate of Dr. Robert S. Stone—he was entrusted with the medical supervision of health and protection of the personnel in several areas of the atomic bomb project.

Cantril's scientific contributions in the field of radiation therapy, nuclear medicine, and radiation protection, published both in medical journals and monographs, are too numerous and too well-recognized in their sincerity, honesty, and thoroughness to be enumerated again. In his modesty, he himself did not consider the many honors, appointments, and formal expressions of recognition bestowed on him here and abroad—while he gratefully appreciated them—as sufficiently important in themselves to mention them in any of his biographical sketches. His true greatness and his impact on the progress of radiation therapy can only be fully appreciated by viewing the whole man.

In his general philosophy he aspired to approach his ideal, Abraham Lincoln, for whom he had the greatest admiration throughout his life. Intellectual integrity, uncompromising honesty towards himself and in the association with others, a relentless striving towards his goals blended with mature understanding of human needs and a warm and sincere, although always realistic and never sentimental, concern for the wellbeing of his fellow men—these were his outstanding characteristics. He spared no effort to help others if he could do so constructively, but he refused to go through futile motions for reasons of expediency. He represented everything noble in American medicine and in American life. In thought and action he was a true democrat with a respect for the individual's integrity—be he friend or foe—regardless of status. He was an ardent but critical patriot, yet a cosmopolitan with a great understanding of European culture and appreciation of European contributions to civilization, to medicine, and to radiology. His broad general education, his thorough interest in literature, history, languages, and music, blended with his pragmatic philosophy of life, made him a true American humanist. In his realistic and determined approach to every task—small or great—he would have agreed with Carlisle's maxim: "Our main purpose is not to see what lies dimly at a distance but to do what lies clearly at hand."

With characteristic determination, Sim Cantril planned and lived his professional life, consistent with his general philosophy. The goal and the road to this goal became clear to him during his apprenticeship with Coutard. His credo, to which he adhered throughout his professional life, is perhaps best expressed in a letter which he wrote from Paris in July, 1936: "A reputation in the last analysis is built on the *clinic*, not on lectures, books, trips. . . . As I see Coutard working, working, working, on the examination of patients, re-examining them, thinking about them, trying new approaches of treatment, analyzing past mistakes and successes, and outlining future therapy, I see that we in America have gone a little too far in the matter of machines and have lost sight of the disease and the clinical approach to it."

From then on it was his purpose to build a pioneer institution in which radiation therapy of cancer could be practiced and taught as a clinical art, based on thorough scientific understanding but guided by careful observation of the patient, as Coutard had taught it. The opportunity came when he was offered the position at the Tumor Institute of the Swedish Hospital. In August, 1938, after his investigation of the Seattle situation, he wrote me: "It looks as though this is an opportunity

to do some good irradiation as I wish, study the 'question' in tranquillity." He recognized that the unusual combination of the available technical facilities, which at that time were unmatched anywhere in the country, with—to him even more important—the freedom of action which the understanding and cooperative staff and board of the hospital offered would provide him with a greater opportunity to accomplish his purpose than would be available in larger institutions with old, established traditions. He therefore refused, during the following years, several flattering offers of positions in large Eastern medical schools and preferred to follow St. Chrysostom's suggestions: "Depart from the highway and transplant thyself in some enclosed ground, for it is hard for a tree which stands by the highway to keep her fruit til it be ripe."

During his years with the Manhattan project and after the war, Cantril was closely associated with the rapidly progressing development of nuclear medicine. He held numerous responsible appointments on committees and governmental agencies and became one of the recognized authorities in the new field of nuclear medicine. Yet—consistent with his characteristic sense of proportion—he was unwilling to organize an isotope department in the Tumor Institute until he was thoroughly convinced of the type of organization needed for clinical purposes and could integrate it accordingly. He refused to be carried to easy fame on a wave of fashionable enthusiasm, as he had resisted this temptation twenty years previously during the early days of supervoltage therapy.

Cantril's real interest remained clinical radiation therapy of cancer, the progressing organization of the Tumor Institute, and the care of his patients. In keeping with his realistic attitude, he was not so much interested in dramatic results in the occasional rare instance of uncommon diseases —although he always had an open mind towards investigating new possibilities and new procedures—as in the improvement of therapy in the more common forms of cancer that had proved to be amenable to curative radiation therapy. His main interest continued to be the treatment of cancers of the cervix and larynx, and he was tireless in his efforts to improve therapy, not by the addition of gadgets but by meticulous, critical self-evaluation. Many of his publications testify to this—to mention here only his monograph on carcinoma of the cervix (1950) and his great critical historical and clinical review of carcinoma of the larynx (1958). It is gratifying to realize that he was permitted to complete this latter publication, his last great scientific contribution, which gave him an opportunity to summarize as only he could have done it the present status of radiotherapy of laryngeal cancer in an objective presentation. It will go down in history as a classic of medical publication and will remain his scientific testament and his last tribute to his great master, Henri Coutard. Cantril's particular gift of viewing any problem in true proportion was perhaps best expressed in his Janeway Lecture of 1957 on "'The Contributions of Biology to Radiation Therapy."

Sim Cantril was primarily a physician. He was born a physician. He was raised in a physician's atmosphere—his father was one of the leading surgeons in the Pacific Northwest. Medicine to him was not a trade, nor even a profession, but a vocation and a way of life. He never lost sight of the guiding principle that the treatment of the patient was the most important element in the treatment of disease, and he practiced and taught consistently that the patient and the the disease was the entity. Obviously, Coutard's insistence on the close observation of the patient and on his reaction under treatment has thus fallen on fruitful soil. Cantril's most important and lasting contribution probably lay in his almost unique ability to integrate in a perfectly balanced fashion a thorough scientific approach in a highly technical specialty with true physicianship. He brought the brilliant but at times impractical ideas of Coutard's genius down to earth and made them useful

for practical medicine. As he matured, he reached the status of a great clinician—well comparable to the clinicians of Osler's and Halsted's type who have become so rare in this generation of technical specialists. To those who were closely associated to him, it was difficult at times to decide what to admire most: his technical skill with attention to minute details—always retaining his sense of proportion; the realization of his responsibility for and never relaxing concern with the wellbeing of the individual patient; or the unemotional but warm interest in the patient's physical, mental and social needs, without consideration of economic or social status. He was uncompromising where the patient's interests were concerned, uncompromising in his demands on himself, his associates, trainees, and other physicians. Medical ethics meant to him, first, meeting the needs of the individual patient.

That in spite of this uncompromising attitude he was admired and respected as the unchallenged leader in his field, even in his own community, is a tribute to his sincerity and tact. His recognition as the outstanding American radiotherapist of his generation was symbolized by his unanimous election as the Founding President of the newly organized American Club of Therapeutic Radiologists at its initial meeting in December, 1958. Abroad, he counted many of the outstanding radiotherapists as his personal friends. They expressed their recognition by electing Cantril as Executive Secretary for North America when the International Club of Radiotherapists was founded in 1952.

The great emotional strain associated with the overwhelmingly heavy responsibilities during his association with the Manhattan Project, together with the at times excessive work during the post-war period when he sometimes carried three full-time jobs simultaneously, undoubtedly contributed to his premature death. Even so, he could not have accomplished what he did if his wonderfully understanding wife had not provided him with a home where he could have at least some—if because of his temperament probably never complete—relaxation. His patients, and all of us who have the interest of the specialty at heart, owe her, too, a great debt of gratitude.

Sim Cantril has completed a purposeful life. He perhaps came closer to the fulfillment of his aspirations than do many of us in a much longer lifetime. In the realization of his early vision, through his own unwavering determination and relentless efforts, he created an institution that implements his philosophy and has become recognized as a leading treatment and teaching center. Through his influence he contributed decisively—perhaps more than any other single man—to the change of atmosphere in the approach to radiation therapy and to its improvement and recognition as a specialty which has become so noticeable in this country during the last decade. He himself would probably consider the creation of his school of clinical radiation therapists as his most important contribution and its perpetuation by those whom he has inspired as his most fitting memorial. For the still struggling field of clinical radiation therapy, his loss creates a void that will be difficult to fill. But the memory of this noble life, of the man and of the physician, will remain with us and continue to exert its influence on his associates, his students, and his many friends, as a living source of inspiration and stimulation.

Franz Buschke, M.D.

SOCIETY PROCEEDINGS AND NEWS ITEMS

MEETINGS OF RADIOLOGICAL SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. C. Allen Good, Mayo Clinic, Rochester, Minn. Annual meeting: Ambassador Hotel, Atlantic City, N. J., Sept. 27–30, 1960.

American Radium Society
Secretary, Dr. Robert L. Brown, Winship Clinic, Emory University, Atlanta 22, Ga. Annual meeting: Caribe Hilton, San Juan, Puerto Rico, March 17–19, 1960.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: December 4–9, 1960, Cincinnati, Ohio.

American College of Radiology
Executive Director, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois. Annual meeting to be announced.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: June 13–17, 1960, Miami Beach, Fla.

American Board of Radiology
Secretary, Dr. H. Dabney Kerr. Correspondence should be directed to Kahler Hotel Building. Rochester, Minn. The spring 1960 examination will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, June 6–10; deadline for filing applications was January 1, 1960. The Fall 1960 examination will be held in Cincinnati, December 5 through 9. The deadline for filing applications is July 1, 1960. A Special Examination in Nuclear Medicine (for diplomates in Radiology or Therapeutic Radiology) will be offered, provided there are sufficient applications.

Tenth International Congress of Radiology
Secretary-General, Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal 2, Quebec, Canada. Meets in Montreal, Aug. 26–Sept. 1, 1962.

Seventh Inter-American Congress of Radiology
Secretary, Dr. Laura Fariñas, Havana, Cuba. *Counselor for the United States*, Dr. J. A. del Regato, Penrose Cancer Hospital, 2200 North Cascade Avenue, Colorado Springs, Colorado. The meeting will be held in Brazil in 1961.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

American Nuclear Society
Executive-Secretary, Octave J. Du Temple, 86 E. Randolph St., Chicago, Ill.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 1313 N. Second St., Phoenix, Ariz. Two regular meetings a year. Annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. J. B. Scruggs, Arkansas Baptist Hospital, Little Rock, Ark. Meets every three months and also at time and place of State Medical Association.

Association of University Radiologists
Secretary, Dr. Paul Riemenschneider, Medical College State University of New York, Syracuse, N. Y. Annual meeting to be announced.

Atlanta Radiological Society
Secretary, Dr. J. L. Clements, Jr., 35 Linden Ave., N.E., Atlanta 8, Ga. Meets monthly, except during three summer months, on second Friday evening.

Blockly Radiological Society
Secretary, Dr. Samuel Finkelman, 101 S. Twentieth St. Philadelphia, Pa.

Brooklyn Radiological Society
Secretary, Dr. George A. Manfredonia, One Hanson Place, Brooklyn, N. Y. Meets first Thursday of each month October through May.

Buffalo Radiological Society
Secretary, Dr. Alfred Dobrak, 710 Leydecker Rd., Buffalo 24, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Radiological Society
Secretary, Dr. Joseph A. Head, 150 Marshall St., Syracuse, N. Y. Meets first Monday each month October through May.

Central Ohio Radiological Society
Secretary, Dr. William B. Schwartz, 1500 W. Third Ave., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, November, January, March and May at Fort Hayes Hotel, Columbus, Ohio.

Central Society of Nuclear Medicine
Secretary, Dr. Robert S. Landauer, Radiation Center Building, 1903 West Harrison St., Chicago 12, Ill.

Chicago Roentgen Society
Secretary, Dr. George B. Cahill, 802 Burns Ave., Flossmoor, Ill. Meets second Thursday of each month, October to April except December at the Sheraton Hotel at 8:00 P.M.

Cleveland Radiological Society
Secretary, Dr. Norman E. Berman, 14404 S. Park Blvd., Shaker Hgts. 20, Ohio. Meetings at 7:00 P.M. on fourth Monday of each month from October to April at Tudor Arms Hotel.

Colorado Radiological Society
Secretary, Dr. Bertram L. Pear, 3705 East Colfax Ave., Denver 6, Colo. Meets third Friday of each month at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. Paul J. Kingston, 114 Woodland St., Hartford, Conn. Meets first Friday in February and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. A. H. Keene, 3707 Gaston Ave., Dallas, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. Kenneth L. Krabbenhoft, Harper Hospital, Detroit 1, Mich. Meets monthly first Thursday, October through May, at David Whitney House, 1010 Antietam, at 6:30 P.M.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

East Tennessee Radiological Society
Secretary, Dr. J. Marsh Frere, Jr., 205 Medical Arts Building, Knoxville, Tenn. Meets in January and September.

Eastern Radiological Society
Secretary, Dr. John D. Osmond, Jr., Euclid-Glenville Hospital, Cleveland 19, Ohio. Meets at Mid Pines Club, Southern Pines, N. C., March 6–10, 1960.

Florida Radiological Society
Secretary, Dr. John P. Ferrell, 166 4th Ave., St. Petersburg, Fla. Meets twice annually, in the spring with the annual State Society Meeting, and in the fall.

*** Secretaries of societies are requested to send timely information promptly to the Editor.**

Florida West Coast Radiological Society
Secretary-Treasurer, Dr. Joseph C. Rush, 1501 Jungle, St. Petersburg, Fla.

Georgia Radiological Society
Secretary, Dr. George W. Brown, Griffin, Ga. Meets in spring and fall with Annual State Society Meeting.

Greater Miami Radiological Society
Secretary, Dr. George P. Daurelle, Jackson Memorial Hospital, Miami 36, Fla. Meets monthly third Wednesday at 8 p.m. at Jackson Memorial Hospital, Miami, Fla.

Greater St. Louis Radiological Society
Secretary, Dr. Harvey A. Humphrey, 462 N. Taylor, St. Louis 8, Mo.

Houston Radiological Society
Secretary, Dr. Edward B. Singleton, 6621 Fannin St., Houston 25, Texas. Meets last Monday each month, Seminar Room, Doctors' Club of Houston.

Idaho State Radiological Society
Secretary, Dr. Charles R. McWilliams, Magic Valley Memorial Hospital, Twin Falls, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. George A. Miller, Carle Hospital Clinic, Urbana, Ill. Meets in spring and fall.

Indiana Roentgen Society
Secretary, Dr. David E. Wheeler, 1500 North Ritter, Indianapolis, Ind. Meets first Sunday in May and during fall meeting of Indiana State Medical Association.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. Lewis G. Allen, 807 Huron Bldg., Kansas City, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. Robert H. Akers, V. A. Hospital, Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. C. P. Naidorf, 411 Parkside Ave. Brooklyn 26, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 p.m.

Los Angeles Radiological Society
Secretary, Dr. Denis C. Adler, 2010 Wilshire Blvd., Los Angeles 57, Calif. Meets second Wednesday of month in September, November, March, April and June at Los Angeles County Medical Association Building, Los Angeles.

Maine Radiological Society
Secretary, Dr. Edward C. Porter, 489 State Street, Bangor, Maine. Meets in June, September, December and April.

Maryland Radiological Society
Secretary, Dr. Nathan B. Hyman, 1805 Eutaw Place, Baltimore 17, Md.

Memphis Roentgen Society
Secretary, Dr. Hollis H. Halford, Kennedy V.A. Hospital, Department of Radiology, Memphis 15, Tenn. Meets first Monday of each month at John Gaston Hospital.

Miami Valley Radiological Society
Secretary, Dr. S. F. Johnson, 2197 Los Arrow Dr., Dayton 9, Ohio. Meets second Friday of fall and winter months.

Mid-Hudson Radiological Society
Secretary, Dr. Joseph Sorrentino, St. Francis Hospital, Poughkeepsie, N. Y. Meets 8:30 p.m., fourth Wednesday each month, September to May.

Milwaukee Roentgen Ray Society
Secretary, Dr. Joseph F. Wepfer, 5000 W. Chambers St., Milwaukee 10, Wis. Meets monthly on fourth Monday, October through May, at University Club.

Minnesota Radiological Society
Secretary, Dr. Donald H. Peterson, 853 Medical Arts Bldg., Minneapolis 2, Minn. Meets three times annually, in fall, winter and spring.

Mississippi Radiological Society
Secretary, Dr. Bernard T. Hickman, University Medical Center, Jackson, Miss. Meets third Thursday of each month at Hotel Edwards, Jackson, at 6:00 p.m.

Montana Radiological Society
Secretary, Dr. J. K. Boughn, 35 11th Ave., Helena, Montana. Meets at least once a year.

Nassau Radiological Society
Secretary, Dr. Jerome Zwanger, 126 Hicksville Rd., Massapequa, L. I., N. Y. Meets second Tuesday of the month in February, April, June, October and December.

Nebraska Radiological Society
Secretary, Dr. Ronald E. Waggener, The Radiologic Center, Nebraska Methodist Hospital, Omaha 31, Nebraska. Meets third Wednesday of each month at 6 p.m. in Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. John E. Gary, 1180 Beacon St., Brookline 46, Mass. Meets third Friday of each month, October through May, at The Longwood Towers, Brookline, Mass.

New Hampshire Roentgen Ray Society
Secretary, Dr. Paul Y. Hasserjian, 1470 Elm St., Manchester, N. H. Meets four to six times yearly.

New York Roentgen Society
Secretary, Dr. William B. Seaman, 622 W. 168th St., New York, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 4:30 p.m.

North Carolina Radiological Society
Secretary, Dr. Owen Doyle, 906 Dover Road, Greensboro, North Carolina. Meets in the spring and fall each year.

North Dakota Radiological Society
Secretary, Dr. R. F. Raasch, Post Office Box 990, Dickinson, North Dakota. Meets at time of State Medical Association meeting. Other meetings arranged on call of the President.

North Florida Radiological Society
Secretary, Dr. Paul A. Mori, 800 Miami Road, Jacksonville 7, Fla. Meets quarterly in March, June, September and December.

Northeastern New York Radiological Society
Secretary, Dr. Irving Van Woert, Jr., Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesday of October, November, March and April.

Northern California Radiological Society
Secretary, Dr. Rob H. Kirkpatrick, 1219 28th St., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

Ohio State Radiological Society
Secretary, Dr. Paul D. Meyer, 125 S. Grant Ave., Columbus, Ohio. Annual meeting to be announced.

Oklahoma State Radiological Society
Secretary, Dr. J. Murphree, 617 E. Brookfield, Ponca City, Okla. Three regular meetings annually.

Oregon Radiological Society
Secretary, Dr. Barbara J. Radmore, 1162 Willamette, Eugene, Ore. Meets monthly from October to June on the second Wednesday of each month at 8:00 p.m. at the University Club.

Orleans Parish Radiological Society
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets second Tuesday of each month.

Pacific Northwest Radiological Society
Secretary, Dr. J. Arch Colbrunn, 19 Royal Oak Drive, Roseburg, Ore. Annual meeting: Vancouver, British Columbia, May, 1960.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco 8, Calif. Meets annually during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. Walter P. Bitner, 234 State St., Harrisburg, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. Robert B. Funch, Department of Radiology, Germantown Hospital, Philadelphia 44, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Charles N. Chasler, 3500 Fifth Ave., Pittsburgh 13, Pa. Meets second Wednesday of month, October through June at Park Schenley Restaurant.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. James K. V. Willson, 1100 N. Charles St., Baltimore 1, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Stanley J. Lucas, 417 Provident Bank, Cincinnati 2, Ohio. Meets monthly from September to May on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. Louis L. Buzaid, The Queen's Hospital, Box 861, Honolulu, Hawaii. Meets third Monday of each month at 7:30 P.M.

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY
Secretary, Dr. Gerhard W. Schottman, 4400 J. C. Nichols Pkwy., Kansas City, Mo. Meets last Friday of each month.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. Seymour Ochsner, Ochsner Clinic, New Orleans 15, La. Meets annually during Louisiana State Medical Society meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Austin J. Tidaback, 912 Prospect Ave., Plainfield, N. J. Meets at Atlantic City at time of State Medical Society meeting and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF NEW YORK STATE
Secretary-Treasurer, Dr Mario C. Gian, 610 Niagara St.. Buffalo 1, N. Y. Annual meeting to be announced.

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA
Secretary-Treasurer, Dr. Donald J. Peik, 303 S. Minnesota Ave., Sioux Falls, S. D.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. Joseph F. Linsman, 436 N. Roxbury Dr., Beverly Hills, Calif.

REDWOOD EMPIRE RADIOLOGICAL SOCIETY
Secretary, Dr. Lee E. Titus, 164 W. Napa St., Sonoma, Calif. Meets second Monday every other month.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Theodore F. Van Zandt, 501 W. Main St., Rochester 8, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Freed, 4200 East Ninth Ave.. Denver 20, Colo. Annual meeting: Denver Hilton Hotel, Denver, Colo., Aug. 11–13, 1960.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets third Wednesday each month in Fort Sam Houston Officer's Club at 6:30 P.M.

SAN DIEGO RADIOLOGICAL SOCIETY
Secretary, Dr. Stanley A. Moore, 2466 First Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

SAN FRANCISCO RADIOLOGICAL SOCIETY
Secretary, Dr. M. A. Sisson, 450 Sutter St., San Francisco 8, Calif. Meets quarterly at Grison's Steak House.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. William H. Graham, 630 East Santa Clara St., San Jose, Calif.

SECTION ON RADIOLOGY, CONNECTICUT STATE MEDICAL SOCIETY
Secretary, Dr. Ralph J. Littwin, Bristol Hospital, Bristol, Conn. Meetings are held bi-monthly.

SECTION ON RADIOLOGY, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. William E. Sheely, 1835 Eye St., N.W., Washington 6, D. C. Meets at Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. William Meszaros, 1825 W. Harrison St., Chicago, Ill.

SECTION ON RADIOLOGY, SOUTHERN MEDICAL ASSOCIATION.
Secretary. Dr. Seymour Ochsner, Ochsner Clinic, 3503 Prytania St., New Orleans 15, La. Annual meeting to be announced.

SHREVEPORT RADIOLOGICAL CLUB
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

SOCIETY OF NUCLEAR MEDICINE
Secretary, Dr. Robert W. Lackey, 452 Metropolitan Bldg., Denver 2, Colo. Annual meeting: Estes Park, Colorado, June 22–25, 1960.

SOUTH BAY RADIOLOGICAL SOCIETY
Secretary, Dr. Stanford B. Rossiter, 1111 University Dr., Menlo Park, Calif. Meets second Wednesday of each month.

SOUTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. Wayne Reeser, 804 Burroughs St., Conway, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

SOUTHERN RADIOLOGICAL CONFERENCE
Secretary, Dr. Marshall Eskridge, Mobile Infirmary, Mobile, Ala.

SOUTHWESTERN RADIOLOGICAL SOCIETY
Secretary, Dr. Gordon Black, Suite 2-A, El Paso Medical Center, 1501 Arizona, El Paso, Texas. Meets second Tuesday of each month.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. James J. Range, P.O. Box 324, Johnson City, Tenn. Meets annually at the time and place of the Tennessee State Medical Association meeting.

TEXAS RADIOLOGICAL SOCIETY
Secretary, Dr. R. P. O'Bannon, 402 Professional Bldg., 1216 Pennsylvania Ave., Fort Worth 4, Texas. Next meeting January 22 and 23, 1960, Houston, Texas.

TRI-STATE RADIOLOGICAL SOCIETY
Secretary, Dr. James R. Mathews, 118 S. E. First St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

UPPER PENINSULA RADIOLOGICAL SOCIETY
Secretary, Dr. A. Gonty, Menominee, Mich. Meets quarterly.

UTAH STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Richard Y. Card, St. Mark's Hospital, Salt Lake City, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. Frank A. Kearney, II, 110 S. Curry St., Phoebus, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Wayne A. Chesledon, 306 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. Karl J. Myers, 112 N. Woods St., Philippi, W. Va. Meets concurrently with Annual Meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. James C. Montieth, 170 Maple Avenue, White Plains, N. Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. Howard G. Bayley, 116 Iroquois Parkway, Beaver Dam, Wis. Annual meeting each spring in various places.

X-Ray Study Club of San Francisco
Secretary, Dr. John H. Heald, 450 Sutter St., San Francisco 8, Calif. Meets monthly, third Thursday at 7:30 p.m., Children's Hospital, September through June.

Cuba, Mexico, Puerto Rico and Central America

Asociación de Radiólogos de Centro America y Panamá
Comprising: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panamá, *Secretary-General*, Dr. Roberto Calderón, Calle Central Deste No. 218, Managua, Nicaragua. Meets annually in a rotating manner in the six countries.

Sociedad de Radiología de El Salvador
Secretary, Dr. Rafael Vega Gómez.

Sociedad de Radiología de Guatemala
Secretary, Dr. Carlos E. Escobar, 9ª. Calle A 0-05, Zona 1, Guatemala.

Sociedad de Radiología y Fisioterapía Cubana
Secretary, Dr. Miguel A. García Plasencia, Hospital Curie, 29 y F, Vedado, Habana, Cuba. Meets monthly at Curie Hospital.

Sociedad Costarricense de Radiologia
Secretary, Dr. James Fernández Carballo, Apartado VIII, San José, Costa Rica.

Sociedad Mexicana de Radiología, A. C.
Calle del Oro No. 15, México 7, D. F.
Secretary-General, Dr. Guillermo Santín. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. R. B. Díaz Bonnet, Suite 504, Professional Bldg., Santurce, Puerto Rico.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sánchez, Apartado No. 6323, Panamá, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Commonwealth of Nations

Association of Radiologists of the Province of Quebec
Secretary, Dr. Odilon Raymond, 5400 Blvd. Gouin. Quest, Montreal, Que. Meets four times a year.

British Institute of Radiology Incorporated with the Röntgen Society
Honorary Secretary, Dr. John Blewett, 32 Welbeck St., London, W. 1. Meets monthly from October until May.

Faculty of Radiologists
Honorary Secretary, Dr. R. A. Kemp Harper, 47 Lincoln's Inn Fields, London, W.C.2, England. Annual meeting: June 10–11, 1960.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London, W. 1.

Canadian Association of Radiologists
Honorary Secretary, Dr. Robert G. Fraser, *Associate Honorary Secretary*, Dr. Jean-Louis Léger, 1555 Summerhill Ave., Montreal 25, Que. Annual meeting to be announced.

Montreal Radiological Study Club
Secretary, Dr. F. McConnell, 1650 Cedar Ave., Montreal, Quebec. Meets first Tuesday evening, October to April.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicale
General Secretary, Dr. Louis Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

Toronto Radiological Society
Secretary, Dr. L. R. Harnick, Toronto Western Hospital, 399 Bathurst St., Toronto, Ontario. Meets second Monday of each month September through May.

College of Radiologists of Australasia
Honorary Secretary, Dr. E. A. Booth, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W., Australia.

South America

Asociación Argentina de Radiología
Secretary, Dr. Lidio G. Mosca, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Ateneo de Radiologia
Secretary, Dr. Victor A. Añaños, Instituto de Radiologia, Santa Fe 3100, Rosario, Argentina. Meets monthly on second and fourth Fridays at 7:00 p.m. in the Hospital Nacional del Centenario, Santa Fe 1300, Rosario.

O Colégio Brasileiro de Radiologia
Secretary-General, Dr. Walter Bomfins Pontes. Seat: Rua Major Quedinho, 99-2°. Andar, São Paulo, Brazil.

Sociedad Argentina de Radiología, Junta Central, Buenos Aires
Secretary, Dr. Edgardo O. Olcese, Santa Fé 1171, Buenos Aires. Meetings are held monthly.

Sociedad Bolivana de Radiología
Secretary, Dr. Javier Prada Méndez, Casilla 1596, La Paz, Bolivia. Meets monthly. General assembly once every two years.

Sociedade Brasileira de Radiologia
Secretary, Dr. Nicola Caminha, Av. Mem. de Sa, Rio de Janeiro, Brazil. General Assembly meets every two years in December.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Chilena de Radiología
Secretary, Dr. Juan Sabbagh Dacla, Merced 565, Santiago, Chile. Meets fourth Friday of each month.

Sociedad Colombiana de Radiologia
Secretary, Dr. Alberto Mejía Diazgranados, Carrera 13, No. 25–31, Apartado aéreo No. 5804, Bogotá, Colombia. Meets last Thursday of each month.

Sociedad Ecuatoriana de Radiología y Fisioterapía
Secretary, Dr. Publio Vargas P., Casilla 1242, Guayaquil, Ecuador.

Sociedad Paraguaya de Radiología
Secretary, Dr. Miguel González Addone, 15 de Agosto 322, Asunción, Paraguay.

Sociedad Peruana de Radiologia
Secretary, Dr. Luis Pinillos Ganoza, Apartado 2306, Lima, Perú. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta 218, Lima.

Sociedad de Radiologia del Atlantico
Secretary, Dr. Raul Fernandez, Calle 40 #41-110, Baranquilla, Colombia. Society meets monthly at the Instituto de Radiologia.

Sociedad de Radiología, Cancerología y Física Médica del Uruguay
Secretary-General, Dr. Ernesto H. Cibils, Av. Agraciada 1464, piso 13, Montevideo, Uruguay.

Sociedade de Radiologia de Pernambuco
Secretary, Dr. Manoel Medeiros, Instituto de Radiologia da Faculdade de Medicina da Universidade do Recife, Caixa Postal 505, Pernambuco, Brazil.

Sociedad Venezolana de Radiología
Secretary-General, Dr. Rubén Merenfeld, Apartado No. 9362, Candelaria, Caracas, Venezuela. Meets monthly third Friday at Colegio Médico del Distrito Federal, Caracas.

Continental Europe

Österreichische Röntgen-Gesellschaft
President, Dr. Konrad Weiss, Mariannengasse 10, Vienna 9, Austria. Meets second Tuesday of each month in Allgemeine Poliklinik.

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 256 Chaussée de Wavre, Heverlee-lez-Louvain, Belgium. Meets in February, March, May, June, October, November and December.

Société Française d'Electroradiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, du Nord, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord. Central Society meets third Monday of each month, except during July, August and September, rue de Seine 12, Paris.
Secretary-General, Dr. Ch. Proux, 9, rue Daru, Paris 8e, France.

Československá Společnost pro Roentgenologii a Radiologii
Secretary, Dr. Robert Poch, Praha 12, Šrobárova 50, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgengesellschaft
Secretary, Professor Dr. med. H. Lossen, Universitäts-Röntgeninstitut. Lagenbeckstr. 1, Mainz, Germany. Annual meeting: May 11–14, 1960.

Società Italiana di Radiologia Medica e di Medicina Nucleare
Secretary, Dr. Ettore Conte, Ospedale Mauriziano, Torino, Italy. Meets annually.

Nederlandse Vereniging voor Electrologie en Röntgenologie
Secretary, Dr. J. R. von Ronnen, Violenweg 14, den Haag, Netherlands.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Española de Radiología y Electrología Médicas y Medicina Nuclear
Secretary, Dr. D. Aureo Gutierrez Churruca, Esparteros, No. 9, Madrid, Spain. Meets monthly in Madrid.

Schweizerische Gesellschaft für Radiologie und Nuklearmedizin (Société Suisse de Radiologie et de Médecine Nucléaire)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

The next list of Meetings of Radiological Societies will be published in the May issue of the Journal.

AMERICAN BOARD OF RADIOLOGY

The Spring 1960 examination will be held at the Terrace Hilton Hotel, Cincinnati, Ohio, June 6 to 10. The deadline for filing applications was January 1, 1960.

The Fall 1960 examination will also be held in Cincinnati, December 5 through 9. The deadline for filing applications is July 1, 1960. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered, provided there are sufficient applications.

THIRD INTERNATIONAL CONFERENCE ON MEDICAL ELECTRONICS

The Electronics and Communications Section of The Institution of Electrical Engineers, in association with the International Federation for Medical Electronics, are organizing the Third International Conference on Medical Electronics which will be held at Olympia, London, July 21–27, 1960.

In conjunction with the Conference, The Institution is promoting an International Scientific Exhibition which will be held at Olympia at the same time as the Conference.

CANCER SEMINAR OF THE PENROSE CANCER HOSPITAL

The Annual Cancer Seminar of the Penrose Cancer Hospital, which is devoted this year to soft tissue lesions, will be reenacted in Puerto Rico on March 16, 1960. Dr. Arthur P. Stout will be the pathologist; Dr. Charles Eckert, the surgeon; Dr. Philip Hodes, the radiologist; and Dr. Juan del Regato, the moderator.

The Puerto Rico Society of Pathologists is sponsoring this Seminar as part of their two-day program. For additional information please write to: Dr. Raúl A. Marcial-Rojas, Professor of Pathology, University of Puerto Rico, San Juan, Puerto Rico.

RADIOLOGICAL PHYSICS COURSE MEMORIAL CENTER, NEW YORK

Announcement of the graduate student program in Radiological Physics offered by the Department of Biophysics of the Sloan-Kettering Institute of Cornell University Medical College is made annually. The curriculum includes formal courses in physics, biology, physiology, chemistry, and radiation physics. Extensive laboratory training in treatment planning, implant dosimetry, application of radioactive isotopes, measurement and calibration of isotopes and other radiation sources, and radiation protection is offered. A thesis is also required for the M.S. degree. A limited number of fellowships are available. Requests for information should be sent to the Department of Biophysics, Sloan-Kettering Institute, Memorial Center, 444 East 68th Street, New York 21, New York.

X-RAY TECHNICIANS TO MEET

The 32nd Annual Convention of the American Society of X-Ray Technicians will be held June 11–16, 1960, at the Netherland Hilton Hotel in Cincinnati, Ohio.

FREEDMAN LECTURES AT UNIVERSITY OF CINCINNATI

On Saturday and Sunday, April 9 and 10, 1960, Dr. John W. Hope, Director of the Department of Radiology, Children's Hospital of Philadelphia, will deliver the 12th Annual Joseph and Samuel Freedman Lectures in Diagnostic Radiology at the University of Cincinnati College of Medicine. There will be no charge for the lectures.

Radiologists desiring to attend are requested to write Dr. Benjamin Felson, X-ray Department, Cincinnati General Hospital, for further details.

We regret to announce the death on November 22, 1959 of Dr. William E. Costolow, a distinguished member of the American Radium Society.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interest of our readers as space permits.

Radiation Biology and Cancer. A Collection of Papers Presented at the Twelfth Annual Symposium on Fundamental Cancer Research at The University of Texas M. D. Anderson Hospital and Tumor Institute. Edited by the Staff of The University of Texas M. D. Anderson Hospital and Tumor Institute. Cloth. Price, $8.50. Pp. 493, with numerous illustrations. The University of Texas Press, Austin 12, Texas, 1959.

Thirty-three papers presented at the Twelfth Annual Symposium on Fundamental Cancer Research in 1958 comprise this volume. Except for several papers on radiation physics and certain clinical applications of radiation, the papers deal primarily with problems of radiobiology. The only aspects of cancer which are considered are those of radiation genesis, except for one paper on the investigation of relative radiosensitivity of several animal tumors under various conditions.

The radiobiologic problems discussed include the relationship of radiation neoplasia and endocrine systems, the investigation of the primary physical and chemical processes operative in radiation effect through study of oxygen effect, linear energy transfer and relative biologic effect, and the induction of neoplasia by ultraviolet light. In the latter case, evidence is presented which is interpreted to mean that the initiation of neoplasia is the result of chromosomal change. Four papers discuss the phenomena of protection of mammals against otherwise lethal doses of whole body irradiation by spleen shielding and by postirradiation transfusions of bone marrow or hematopoietically active spleen or fetal liver and the consequences of such induced recovery, a field of special interest currently.

Six papers are devoted to radiation carcinogenesis in animals and man by acute and chronic external irradiation as well as by internally administered isotopes. One paper discusses the relationship of mutagenesis and carcinogenesis, concluding that no proof is available at present for the somatic mutation hypothesis of cancer causation. The results of an investigation of the problem of genetic interaction between tumor viruses and host cells are presented in one paper; a second reports the finding by electron microscopy of virus-like structures in a mouse leukemia caused by cell-free material from a roentgen-ray induced leukemia but not in the latter. In a paper on radiation and human genetics, an excellent discussion is given on the mutagenic effect of radiation on man and the difficulties encountered in extrapolating from experimental evidence in infrahuman forms to human populations.

Although many of the papers are of interest primarily to investigators working in the various fields, much general information can be gleaned by those with less specific interests. A reading of this volume certainly provides insight into the complexities of research in radiobiology and into the fragmentary and incomplete state of existing knowledge in this field.

Isadore Lampe, M.D.

Regeneration in Vertebrates. Edited by Charles S. Thornton. Cloth. Price, $3.25. Pp. 108, with numerous illustrations. The University of Chicago Press, 5750 Ellis Avenue, Chicago 37, Illinois, 1959.

This is one of ten volumes on developmental biology and is the result of conferences held under the auspices of the National Academy of Sciences and the National Research Council. Condensed versions of six conferences (1956) on the regeneration of the eyes, tail, and limbs in amphibia are presented, together with discussions. References for each paper are provided. The chairman was E. G. Butler.

The following topics are covered by various authors. L. S. Stone discusses the regeneration of the iris, lens, and neural retina from the retinal pigment epithelium. The lens can regenerate from the iris in the presence of neural retina. H. Holtzer compares the regeneration of the tail with the embryogenesis of axial structures in vertebrates in general. D. T. Chalkley deals with the source of the cells involved in limb regeneration. M. Singer emphasizes the necessity of nerves for limb regeneration. Al-

though limbs regenerate in tadpoles, they do so in frogs only when the number of nerve fibers at the amputation surface is increased artificially. This raises the interesting possibility of producing regeneration in higher forms. There is a brief discussion of the role of hormones in regeneration. The chapter of greater interest to readers of this *Journal* concerns the effect of roentgen rays on regenerative capacity. H. A. L. Trampusch points out that regeneration is inhibited if the limb has been irradiated (1,000 r) prior to amputation. If nonirradiated tissues (skin, bone, muscle, or nerve) are transplanted to the amputation site, however, regeneration can occur.

R. O'Rahilly, M.D.

Therapie mit Röntgenstrahlen und radioaktiven Stoffen. By Dr. H.-J. Fiebelkorn, Oberarzt am Universitäts-Strahleninstitut Marburg/Lahn, jetzt Chefarzt der Abteilung für Röngendiagnostik und Strahlentherapie am Stadtkrankenhaus Rüsselsheim/Main; and Prof. Dr. W. Minder, Professor für medizinische Strahlenphysik an der Universität Bern, Leiter des Radium-Institutes. Cloth. Price, DM 43.–. Pp. 434, with numerous illustrations. Verlag Hans Huber, Bern, Switzerland; Intercontinental Medical Book Corporation, 381 Fourth Avenue, New York 16, N. Y., 1959.

This book covers the field of radiotherapy, including radium therapy. After a short introduction, the authors proceed to a discussion of the treatment of individual lesions grouped under nervous diseases and dermatologic diseases. Then follows a section on the practical applications of the medium and high dosage treatment of benign and malignant tumors.

The second half of the book deals with the physical aspects of radiation and dosimetry, with special emphasis on dosimetry. There is a short section devoted to isotopes.

James T. Case, M.D.

The Mediastinum. By Ted F. Leigh, M.D., Professor of Radiology, Emory University School of Medicine; Director of the Department of Radiology, Emory University Hospital; and H. Stephen Weens, M.D., Professor of Radiology and Chairman of the Department of Radiology, Emory University School of Medicine; Director of the Department of Radiology, Grady Memorial Hospital, Atlanta, Georgia. Cloth. Price, $11.50. Pp. 246, with 290 illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1959.

Many excellent texts are now available dealing with medical, surgical, and radiologic aspects of chest disease. Most of these devote considerable space to mediastinal pathology. This does not render the present book superfluous. The concise and profusely illustrated text should be a welcome aid to the physician confronted with an undiagnosed mediastinal tumor.

The book is presented from the viewpoint of the diagnostic radiologist with lesions from the most common to the most rare being discussed in detail. Two chapters present detailed description of gross and radiologic anatomy. Both the illustrations and diagrams are excellent and good bibliographies accompany each chapter. Differential diagnostic signs and procedures are referred to throughout.

Arch H. Hall, M.D.

Cancer: Diagnosis and Treatment. Edited by John B. Field, M.D., Ph.D., Assistant Clinical Professor of Medicine, University of Southern California School of Medicine, Los Angeles, California. With 28 contributors. Cloth. Price, $18.50. Pp. 796, with numerous illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, Mass., 1959.

This work is an eclectic appraisal of the genealogy, detection and therapeutic response of malignant neoplasia. Twenty-eight well-known specialists contribute to twenty chapters, all of which are anatomically compartmented except those outlining cancer in children, chemotherapy, radiotherapy and medical aspects of supportive care. It is largely a reaffirmation of faith in classic concepts of tumor behavior and response in which some of the predicating statistical samplings differ significantly from those of other well documented investigations proposing different patterns. The surgical approach is accentuated, although most of the standard and some of the more newly proposed radiation techniques are summarized.

Two chapters emerge preeminent: "Tumors of the Breast" and "Tumors of the Female Generative Tract." Each provides a skillful assay of the incident cancers, and what can be reasonably accomplished in the various clinical stages of these neoplasms. Iatrogenic reactions, heroic and intractable, and the difference between

what is done to and what is done for the cancer patient receive some exploration.

The book may be of selective interest to the surgical specialist or radiotherapist but, as a corollary to its compact, comprehensive packaging, it will be of most value to the general medical practitioner.

James J. Snider, M.D.

Atomic Medicine. Edited by Charles F. Behrens, M.D., F.A.C.R., Rear Admiral, MC, U. S. Navy, (ret.); Roentgenologist, Yater Clinic, Washington, D. C.; Consultant and Lecturer in Radiology, U. S. Naval Medical Center, Bethesda, Maryland; Formerly: Director, Atomic Defense Division, Bureau of Medicine and Surgery, Navy Department; Commanding Officer, Navy Medical Research Institute, National Naval Medical Center, Bethesda, Maryland. Third Edition. Cloth. Price $15.00. Pp. 705, with numerous illustrations. The Williams & Wilkins Company, Mount Royal and Guilford Avenues, Baltimore 2, Maryland, 1959.

To bring together under one cover in comprehensive survey form the myriad of general and semitechnical data concerning the uses of atomic energy was the motivation for the first edition of this work in 1949. That this, the third edition, was called for attests that its goal was achieved and that it was well received. An indicator of the changing times we live in is the subject matter that was extensively revised or expanded to make this edition as current and complete as possible: radiation hazards of atomic weapons, acute whole body irradiation effects, skin lesions from fallout, internal effects of radioisotopes, medical aspects of radioactive tracer substances and their practical administration, particle acceleration, and research.

The various chapters in the book are written by outstanding radiologists, radiation biologists, physicists, pathologists and allied medical specialists, each an expert on the topic under discussion. The 705 pages and 24 chapters cover subject matter ranging from a general background of atomic medicine through detailed discussions of atomic physics, nuclear reactors and weapons, radiation biology and pathology, diagnosis and therapy of acute radiation injuries, internal and external effects of radioisotopes and fallout, radiation protection and survival methods in atomic disaster, particle accelerators, medical uses of radioisotopes and their practical handling, radiation in dentistry, and enlightenment on some pertinent results from recent research. The material is presented in an easy, readable style with numerous illustrations and simple diagrams for the basic orientation of the novice, but is also complete with medical charts, graphs and formulae for general reference work and detailed study. For the reader or researcher whose interest craves additional study material, a detailed bibliography at the end of each chapter is available for endless ramifications.

This book is recommended to anyone who desires a comprehensive review of the field of atomic medicine, enabling him to put its many facets in their proper perspective; it should be of special interest to radiologists, pathologists, internists, physicists and ancillary medical workers who use ionizing radiations or are involved in planning for the care of radiation casualties.

Donald M. Monson, M.D.

BOOKS RECEIVED

Annual Review of Nuclear Science. Volume 9. Edited by Emilio Segrè, University of California; and Leonard I. Schiff, Stanford University; and Associate Editors Gerhart Friedlander, Brookhaven National Laboratory; and Walter E. Meyerhof, Stanford University. Cloth. Price, $7.00. Pp. 625, with numerous illustrations and tables. Annual Reviews, Inc., 231 Grant Avenue, Palo Alto, Calif., 1959.

Cinefluorography. Proceedings of the First Annual Symposium on Cinefluorography, Sponsored by the Department of Radiology, University of Rochester School of Medicine and Dentistry, Rochester, New York, Friday and Saturday, November 14 and 15, 1958. Edited by George H. S. Ramsey, M.D., Professor and Chairman; James S. Watson, Jr., M.D., Research Professor; Theodore A. Tristan, M.D., Senior Instructor; Sydney Weinberg, Research Associate; and William S. Cornwell, M.A., Clinical Associate; all from the Department of Radiology, University of Rochester School of Medicine and Dentistry. Cloth. Pp. 266, with numerous illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1959.

The Treatment of Bronchial Neoplasms. Publication No. III in The John Alexander Monograph Series on Various Phases of Thoracic Surgery. By Robert R. Shaw, M.D.; and Donald L. Paulson, M.D.; with a chapter on Bronchial Adenoma by John Lester Kee, Jr., M.D.; all from the Southwestern Medical School of the University of Texas and Baylor University Hospital, Dallas, Texas.

Cloth. Price, $8.00. Pp. 135, with numerous illustrations. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1959.

Roentgenologic Diagnosis in Ophthalmology. By Edward Hartmann, M.D., Chief of the Ophthalmic Department, Lariboisière Hospital and American Hospital in Paris; and Evelyn Gilles, M.D., Chief of the Roentgenology Department, Quinze-Vingt Ophthalmic Hospital; Associate in Roentgenology, Saint Antoine Hospital and American Hospital in Paris. Cloth. Price, $15.00. Pp. 357, with 497 illustrations. J. B. Lippincott Company, East Washington Square, Philadelphia 5, Pa., 1959.

Medieval and Renaissance Medicine. By Benjamin Lee Gordon, M.D., F.I.C.S. Cloth. Price, $10.00. Pp. 843. Philosophical Library, Inc., 15 East 40th Street, New York 16, N. Y., 1959.

Radiation Biology of Vicia Faba in Relation to the General Problem. By John Read, B.Sc., Ph.D., the Hugh Adam Research Department of the Medical School and the New Zealand Branch of the British Empire Cancer Campaign, University of Otago, Dunedin, New Zealand. Cloth. Price, $10.50. Pp. 270, with 74 illustrations and 41 tables. Charles C Thomas, Publisher, 301–327 East Lawrence Avenue, Springfield, Ill., 1959.

Medical X-Ray Technique; Principles and Applications. By G. J. van der Plaats, Chief Radiologist of the X-Ray Department at St. Annadal Hospital, Maastricht, and former Professor of Radiology in the University of Groningen. Cloth. Price, $10.00. Pp. 480, with 213 illustrations. The Macmillan Company, 50 Fifth Avenue, New York 11, N. Y., 1959.

The Year Book of Radiology (1959–1960 Year Book Series). Edited by John Floyd Holt, M.D., Professor, Department of Radiology, University of Michigan; Walter M. Whitehouse, M.D., Associate Professor, Department of Radiology, University of Michigan; Harold W. Jacox, M.D., Professor of Radiology, College of Physicians and Surgeons, Columbia University; Chief, Radiation Therapy Division, Radiologic Service, Presbyterian Hospital, New York City; and Morton M. Kligerman, M.D., Professor of Radiology and Chairman of the Department of Radiology, Yale University School of Medicine; Radiologist-in-Chief, Grace-New Haven Community Hospital. Cloth. Price, $10.50. Pp. 446, with 328 illustrations. Year Book Publishers, Inc., 200 East Illinois Street, Chicago 11, Ill., 1960.

The Human Spine in Health and Disease. First American Edition. By Georg Schmorl, M.D.; and Herbert Junghanns, M.D. Translated and edited by Stefan P. Wilk, M.D.; and Lowell S. Goin, M.D. Cloth. Price, $21.00. Pp. 285. with 419 illustrations. Grune & Stratton, Inc., 381 Fourth Avenue, New York 16, N. Y., 1959.

Strahlenbiologie, Strahlentherapie, Nuklearmedizin und Krebsforschung; Ergebnisse 1952–1958. Edited by H. R. Schinz; H. Holthusen; H. Langendorff; B. Rajewsky; and G. Schubert. Cloth. Price, $65.50. Pp. 998, with numerous illustrations and tables. Georg Thieme Verlag, Herdweg 63, Stuttgart, Germany, 1959. In the U.S.A. and Canada, Intercontinental Medical Book Corporation, New York 16, N. Y.

The Scandinavian Journal of Clinical & Laboratory Investigation. Vol. 11—Supplementum 42. Studies on the Content of 17-Hydroxycorticosteroids and Its Diurnal Rhythm in the Plasma of Surgical Patients. By Björn Thomasson. Paper. Pp. 180. University of Turku, Turku (Åbo), Finland, 1959.

The Scandinavian Journal of Clinical & Laboratory Investigation. Vol. 11—Supplementum 43. The Urinary Excretion of Free Amino Acids and Other Amino Compounds by the Human. By Otto Rudolf Jagenburg. Paper. Pp. 183, with 25 illustrations and 46 tables. University of Göteborg, Göteborg, Sweden, 1959.

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ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. Leucutia, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Jupe, M. H. Hydrocephalus; the Skinner Lecture, 1958. *J. Fac. Radiologists*, July, 1959, *10*, 119–129. (From: Department of Radiology, The London Hospital, London E.1, England.)

Hydrocephalus can be hypertensive (internal or obstructive, and communicating) or compensatory, with increased pressure only in the former. Hypertensive hydrocephalus results from: (a) increased formation of fluid; (b) impaired absorption of fluid; and (c) obstruction to fluid outflow. In compensatory hydrocephalus there is an increase in the quantity of cerebrospinal fluid to fill up the space resulting from atrophy, shrinkage or scarring of the brain.

Roentgen appearance without contrast material. In the hypertensive patient with internal or obstructive hydrocephalus before the sutures are firmly united, the bones of the skull may separate owing to opening of the sutures. Usually, it is only when a mild, but sustained, obstruction arises in an individual young enough to have convolutional markings normally present that these markings are perpetuated into adulthood. In the adult, when the skull bones are already fused, the earliest and most reliable evidence is thinning of the dorsum sellae. Later, the pituitary fossa may be deepened and the dorsum sellae may become eroded from above, downward, by pressure from the anterior end of the dilated third ventricle. With any great increase of pressure, holes may appear in the floor of the middle fossa due to thinning, and in such a case cerebrospinal rhinorrhea may occur. In young individuals the orbital roofs may be depressed causing proptosis.

Roentgenologic evidence of dilatation of the ventricles after the injection of contrast medium. At present air injection into the ventricles is the surest method of investigating hydrocephalus, especially for deep and obstructive lesions. The earliest sign of ventricular dilatation is rounding of the upper and outer angles of the lateral ventricles in the anteroposterior view.

The causes of hydrocephalus are grouped by the author under the following headings: malformations, inflammations, parasites and infections, toxic hydrocephalus, neoplasms and other space-occupying lesions, and atrophy of the brain.—*Samuel G. Henderson, M.D.*

Steinbach, Howard L., Feldman, Robert, and Goldberg, Minnie B. Acromegaly. *Radiology*, April, 1959, *72*, 535–549. (Address: H. L. Steinbach, Department of Radiology, University of California Medical Center, San Francisco 22, Calif.)

The pathology, physiology, and roentgen findings in acromegaly are discussed by the authors. Acromegaly is the result of an increase in size and function of the eosinophilic cells of the anterior pituitary either by hyperplasia of these cells or, more commonly, by an eosinophilic adenoma. This disease produces signs and symptoms by the expansile growth of the pituitary neoplasm, the production of excessive amounts of pituitary hormone, and the interference with normal pituitary function by pressure of the tumor on the uninvolved gland.

The excessive production of growth hormone affects all the tissues of the body by hyperplasia or hypertrophy. There is an increase in connective tissue producing the characteristic thickening of the skin. Thickening of cartilage, synovia, bursae, ligaments, and bone leads to a generalized enlargement of the joints. If the bones are affected prior to epiphyseal union, there is a marked increase in tubular bone length causing gigantism. Usually, however, the disease has its inception after puberty so that there is only a minor increase in height. There are areas where endochondral growth may continue after puberty, such as the mandibular condyle, and this causes the characteristic mandibular elongation and prognathism so commonly seen in this disease. The same process may occur at the costochondral junction and produces elongation of the ribs with resultant increase in chest cavity size and kyphosis. Bone growth as the result of periosteal apposition is even more pronounced in areas where bone growth continues normally throughout life, such as spur formation about the joints occurring at an early age, and a general increase in bone thickness, such as occurs in the calvarium, vertebrae, phalanges, facial and long bones. Localized resorption of bone is also observed, as in the enlargement of the paranasal sinuses. In males, this produces the supraorbital bulging seen in the frontal sinus area. The mastoid processes and air cells increase in size by a similar process. There is an excessive modelling resorption seen particularly in the proximal phalanges and metatarsals of the feet. Splanchnomegaly also occurs due to connective tissue proliferation and hyperplasia of the differentiating functional cells.

The roentgen findings of 27 acromegalics are tabulated with particular reference to differences between the sexes. The usual sex differences in soft tissue and skeleton were found to be exaggerated in this disease. The sella turcica was abnormal in all but 3 of the 27 patients with either enlargement, invasion into the sphenoid sinus, or extension by the tumor upward above the diaphragma sellae. Calvarial thickening and hyperostosis frontalis were more common in the females, whereas thickening of the scalp tissue and enlargement of the frontal sinuses were more common in males. There was an associated marked exaggeration of the posterior concavity of the vertebral bodies as is usually seen with spinal cord tumors. The thorax was enlarged due to rib elongation. The most frequent abnormality of the hands and feet was a marked thickening of the soft tissues of the digits, particularly prominent

about the proximal interphalangeal joints of the fingers. The tufts of the terminal phalanges were enlarged in the majority of these patients, mostly in the males. Exostoses were present in the periarticular surfaces of the ends of the bones, especially the metacarpal heads. A constriction of the shafts of the proximal phalanges and metatarsal bones of the foot was often observed and, as this is seen in few normal subjects, a roentgenogram of the feet should be obtained along with the skull and hands in the routine evaluation of acromegaly.

Effectiveness of therapy was gauged by the diminution in thickness of the soft tissues. This was felt to be due to a loss of the characteristic edema. In a few patients a reduction of the size of the sella was noted, although none returned to normal size.

The authors stress the fact that the diagnosis of acromegaly is primarily a clinical one. The combination of all the classic features of acromegaly was found in only a few of the patients studied and the diagnosis by roentgen means alone would not have been possible in many cases.—*John S. Alexander, M.D.*

Voluter, George. The V-test. *Radiol. clin.*, 1959, suppl. 28, 5–17. (From: Department of Radiology, M. D. Anderson Hospital and Tumor Institute, University of Texas, Houston, Tex.)

This paper is the result of thirty years' research. Its originality lies in the proposition that the sella turcica and base of the cranium represent a means of identifying victims of catastrophic death. These structures contain features as distinctive individually as fingerprints. They are confined to a simple, limited portion of the body and yield a maximum amount of information and certainty of identification in a minimum time.

The author mentions the liner "Noronic" which burned in Toronto, cremating 119 people. The tremendous task of identifying the unbelievably mutilated and entirely unrecognizable bodies took four months and many complicated methods. Examination of dental remnants was disappointing, as the jaw bones as well as dentures were destroyed by fire in 87 victims. Finger print examination was nearly impossible because of the effect of such destructive forces.

The author's test, so-called because his name begins with a "V," employs the base of the cranium. It is striking to see that even in the most charred bodies it remains intact; the brain mass protects it against the worst injuries. The method entails obtaining *in vivo* roentgenograms of the cranial base of those engaged in hazardous work. Comparing postmortem roentgenograms of skulls with those taken *in vivo*, distinctive criteria would include: (1) the shape and volume of the sella turcica; (2) the angle formed by the basilar plane and the plane of the anterior cranial fossa; (3) morphologic properties of the clinoid processes, bony bridges and osteophytes; (4) characteristic bone structure and pneumatization of the sellar mass; and (5) the size and shape of the sphenoid sinus.

Supporting this well written article with appropriate diagrams and charts, the author recommends the establishment of radio-anthropomorphic files for the Army, Navy, Air Force, police, insurance companies, industries, etc.—*David C. Alftine, M.D.*

Garcia Oller, Jose L., and Tartell, Paul. Incidence of ventricular and subarachnoid filling in fractional encephalography. *South. M. J.*, Sept., 1959, *52*, 1041–1047. (From: Roosevelt Hospital, New York, N. Y.)

This is a report of 55 consecutive encephalographies performed with the fractional technique of Lindgren. With the patient erect and the head slightly flexed, 8 cc. of air is injected slowly. Posteroanterior and lateral encephalograms are made and studied. The subsequent procedure depends upon the initial result. If no air has entered the ventricles, the head is slightly extended, additional air is injected and the roentgenography in the two projections is repeated. If ventricular filling is adequate, a third injection of 8 cc. of air is made with the head and neck in maximum flexion in order to fill the dorsal cerebellar and collicular cisterns. Posteroanterior and lateral encephalograms are again taken and studied. If satisfactory, no more air is injected; the head is extended maximally; and roentgenography in the same projections is repeated. In the average patient a total of 24 cc. of air is injected.

The ventricular system was adequately filled in 54 of the 55 patients. Controlled and selective filling of the basilar cisterns and convexity was possible in most cases. There was filling of the anterior cisterns in 98 per cent, filling of the cisterna ambiens in 82 per cent, filling of the cerebellar cisterns in 88 per cent, and filling of the convex spaces in 82 per cent.

The disadvantages of the procedure are the time consumed and the large number of films used. The advantages are selective filling of the areas desired and excellent visualization of the posterior fossa.—*J. L. Williams, M.D.*

Shapiro, Robert, and Robinson, Franklin. Controlled fractional pneumoencephalography; with particular reference to technic and the anatomy of the subarachnoid cisterns. *Radiology*, May, 1959, *72*, 651–664. (Address: R. Shapiro, Hospital of St. Raphael, New Haven 11, Conn.)

It is generally agreed that pneumoencephalography provides more information than ventriculography in most cases, with little risk to the patient. A technique for controlled fractional pneumoencephalography is described. Special emphasis is placed

on the positioning of the head, since, with the patient in the sitting position and the head in the ideal position of moderate flexion, the gas injected into the lumbar subarachnoid space ascends to the anterior central portion of the cisterna magna and then passes through the foramen of Magendie to the fourth ventricle, aqueduct, and posterior portion of the third ventricle. Whereas, with the head in more flexion, or in the neutral or extended position, the gas passes into other portions of the cranial subarachnoid space and does not reach the ventricular system. After the escape of a few drops of spinal fluid from the lumbar puncture needle, 6 to 8 cc. of air is injected slowly. Posteroanterior and lateral roentgenograms are made with the position of the head unchanged, after which any correction in the position of the head may be made if necessary and ventricular filling again checked after the introduction of another 6 to 8 cc. of air. Finally, an additional 10 to 15 cc. of air is introduced after the removal of slightly less spinal fluid. The last 5 cc. of air is injected with the head slightly extended to insure filling of the ventral basilar cisterns. An additional 5 to 10 cc. of air is injected with the head in marked flexion if it is desirable to visualize the sulci over the cerebral hemispheres. The total amount of air routinely employed rarely exceeds 20 to 30 cc. Successful ventricular filling can be achieved 90 per cent of the time. Once satisfactory filling is obtained additional roentgenograms are made in various positions to demonstrate the ventricular system and subarachnoid cisterns.

In recent years the importance of the subarachnoid cisterns in the diagnosis of various intracranial lesions has been recognized. The anatomy of the subarachnoid cisterns is reviewed, the knowledge of which will make possible the recognition of cisternal deformities and thereby facilitate early and accurate diagnosis. This is particularly true in the differential diagnosis of tumors in the sellar region and in the posterior fossa, and in the recognition of herniation of the cerebellar tonsils and the cerebral peduncles.

Pneumoencephalography fails in 5 to 10 per cent of cases, a small fraction of failures being due to various minor anatomic abnormalities of the cisterna magna. If one excludes these anomalies and improper technique, unsuccessful ventricular filling is usually due to an obstruction to the upward flow of gas, particularly in patients with increased intracranial pressure. This is the prime indication for ventriculography. As a safety measure burr holes should be made prior to pneumoencephalography in patients with increased intracranial pressure so that no time is lost if it becomes necessary to do a ventricular puncture.—*Walter H. Jarvis, Jr., M.D.*

Palubinskas, A. J., and Davies, Hugh. Roentgen features of nasal accessory sinus mucoceles. *Radiology*, April, 1959, *72*, 576–584. (Address: A. J. Palubinskas, Lysholm Radiological Department, The National Hospital, Queen Square, London W.C.1, England.)

The clinical and roentgenologic findings observed in 13 cases of mucoceles of the paranasal sinuses are reported by the authors. Six cases are presented in chart form. Two cases of the 13 are examples of rare sphenoid sinus mucoceles.

The majority of mucoceles occurs in the frontal and ethmoid sinuses, most commonly in the former. They rarely are observed in the sphenoid or maxillary sinuses. Suggestive causative factors are legion, but the exact etiology is unknown. The usual clinical findings are those of a slowly growing painless swelling of the forehead or the nasofrontal region of the orbit just along the inner canthus, with swelling and ptosis of the upper eyelid. Proptosis, usually mild to moderate, is common. Diplopia, blurring or diminution of vision, epiphora or smarting of the eyes occurs. Headache or pain in the region of the swelling or in the eye may be present.

The roentgenologic findings are the changes produced by the mucocele as it expands within the involved sinus. The septate and scalloped normal contour of the sinus is changed into a smooth margin, particularly noticeable in the frontal sinuses. The surrounding bony walls may become osteosclerotic or osteoporotic. The sinus increases in size, and may vary in translucency. These findings are not pathognomonic of a mucocele. Any slowly growing noninvasive lesion which expands and produces pressure atrophy of the wall of a sinus may produce any of these findings; however, the presence of a combination of these changes makes the diagnosis of mucocele likely.—*W. M. McBride, M.D.*

Gros, C., Vlahovitch, B., and Roilgen, A. (Montpellier, France.) Les arrêts circulatoires dans l'hypertension intra-cranienne suraiguë. (Circulatory arrests in very acute intracranial hypertension.) *Presse méd.*, May 27, 1959, *67*, 1065–1067.

The authors previously published a paper on 7 cases of acute intracranial hypertension. They present 4 new cases and their observations on experimentally produced intracranial hypertension in a cat.

Absence of visualization of intracranial vessels by carotid or vertebral arteriography is explained as being due to mechanical obstruction caused by marked imbalance between the increased intracranial and the decreased general, systemic arterial tensions. Reflex spasm of intracranial vessels could also be a minor factor in certain cases of arrest of intracranial circulation.—*Jirair N. Sarian, M.D.*

Neck and Chest

Canepa, Hugo Saravia. Bocio intratoracico congenito. (Congenital intrathoracic goiter.)

Prensa méd. argent., Mar. 6, 1959, *46*, 587–591. (Address: Avenida Belgrano 1032, Salta, Argentina.)

Congenital intrathoracic goiters are rare. These goiters arise from the aberrant embryologic rests. When surgery is contemplated, they must be distinguished from the substernal extension of an enlarged thyroid in the neck because the surgical approach is through the thorax. These goiters may be asymtomatic and may be found accidentally at autopsy or in routine roentgen examination.

Depending upon the structures involved, the symptoms may present themselves as respiratory difficulty, alterations in cardiovascular function, difficulty in swallowing, nervous symptoms, etc. The basal metabolic rate is increased. Roentgenologically, a barium examination of the esophagus shows the relationship of the trachea to the goiter. Radioiodine can be used to test the function and location of the tumor. Other diagnostic aids include bronchoscopy and angiography. In the differential diagnosis, asthma, cardiac disease, cardiospasm and anterior mediastinal tumors should be considered.

The case of a sixty-five year old woman complaining of difficulty in swallowing solid food, dyspnea on exertion and cyanosis is presented. Roentgenologically, there was evidence of compression of the trachea and esophagus above the tracheal bifurcation by a superior mediastinal tumor. Under general anesthesia the tumor was removed. Histologically it was found to be a simple colloid goiter.—*Murray M. Friedman, M.D.*

Roisinblit, Aldolfo, Anunziato, Luis, and Garcia, Willis E. Estafilococia pulmonar; estudio clinico, radiológico y terapéutico. (Staphylococcus pneumonia; clinical, roentgenologic and therapeutic study.) *Prensa méd. argent.*, Mar. 13, 1959, *46*, 630–638. (Address: A. Roisinblit, Remedios E. de San Martin 3068, Lanús, Buenos Aires, Argentina.)

Three cases of staphylococcus pneumonia are presented. This condition which is relatively common in infancy is rare in adults; however, its increasing frequency can be explained by the general use of antibiotics and the development of resistant bacteria.

Staphylococcus pneumonia can be considered an important cause of acute pulmonary disease in the adult. Roentgenologic examination shows characteristic changes but they cannot be said to be pathognomonic. In general they include pneumothorax, formation of pneumatoceles, varying degrees of infiltration with perifocal emphysema, encapsulated pleural collections and enlargement of hilar shadows.

In the majority of cases the diagnosis is made from the clinical picture, which resembles that of other types of severe pulmonary disease, and from the sputum which contains staphylococci or other bacteria. These cases respond only partially to modern antibiotic therapy. Sigmamycin intravenously administered proved to be efficacious in the reported cases.—*Murray M. Friedman, M.D.*

Meyers, Harvey I., and Jacobson, George. Staphylococcal pneumonia in children and adults. *Radiology*, May, 1959, *72*, 665–671. (Address: H. I. Meyers, 1200 North State St., Los Angeles 33, Calif.)

Staphylococcal pneumonia has become an increasing problem in children, particularly in infants under six months of age. Since 1950, 76 proved cases of pneumonia due to *Staphylococcus aureus* have been seen at the Los Angeles County Hospital. Almost one half of the cases were less than six months of age. The mortality rate in this group was slightly over 50 per cent. The only way mortality can be reduced is by the earliest possible diagnosis and proper therapy.

The roentgenologic findings in staphylococcal pneumonia serve to distinguish it from all other types of pneumonia, especially in infants and small children. One of the most striking characteristics of the disease is the rapid change in the roentgen findings. The picture may change from one of minimal to very extensive involvement in a matter of hours. There is little correlation between the roentgenologic appearance and the clinical condition of the patient. The pneumonic infiltration may be lobar or segmental in distribution. Rarely, the infiltration is bilateral. Pleural effusion or empyema is a common occurrence and its presence in a young infant is nearly pathognomonic. Pneumatocele formation is common, usually appearing late in the course of the disease. The pneumatoceles are thin-walled cyst-like areas, which may or may not contain air fluid levels, and tend to change rapidly in size, shape and location. Pyopneumothorax is another characteristic finding.

The picture in adults is not so clear cut. In the older group infiltration is a more prominent feature. Empyema is less common and less extensive. Pneumatoceles are present less frequently, but true lung abscesses are seen much more commonly than in children.

The course of the disease is frequently prolonged, often requiring several months of active treatment. Most of the organisms in patients who were successfully treated were sensitive to chloramphenicol, erythromycin, or bacitracin.—*A. W. Sommer, M.D.*

Fanconi, G. The differential diagnosis of interstitial lung disease in childhood. *German Med. Monthly*, July, 1959, *4*, 219–222; *Deutsche med. Wchnschr.*, 1959, *84*, 709. (Address: Universitäts-Kinderklinik, Steinwiesstr. 75, Zürich 7, Switzerland.)

The marked decline in bacterial lung disease re-

sulting from the use of chemotherapy and antibiotics has caused the interstitial lung diseases to assume a more prominent role in pediatrics. The author briefly reviews the etiology, pathology, clinical findings and roentgen findings in this group of diseases. A summary of cases based on the classification of Uehlinger and Schoch is also presented in this interesting and informative article.

The author indicates the differential diagnoses to be considered in the following subacute and chronic interstitial lung diseases:

A. *Physicochemical interstitial processes:* 1. pulmonary fibrosis following bronchography; 2. lipoid pneumonia.

B. *Interstitial lung diseases caused by infective organisms:* 1. atypical pneumonias with a lingering course (virus pneumonia); 2. constitutional diseases, *e.g.* mucoviscidosis (peribronchitis and bronchiectasis); 3. "conditional" forms, *e.g.* interstitial plasma cell pneumonia (premature babies attaining the age of two to three months); 4. lung lesions in cytomegaly (Hecht's disease); 5. eosinophilic pertussoid pneumonia of infancy (Botsztejn); 6. diffuse progressive interstitial fibrosis of the lungs (Hamman-Rich).

C. *Hypersensitivity reactions of the interstitium of the lung:* 1. collagen diseases (fibrinoid degeneration of the collagenous fibers and/or the amorphous ground substance; entry of protein which has become foreign to the body): (a) rheumatic pneumonia, (b) fibrosis of the lung in lupus erythematosus disseminatus, (c) fibrosis of the lung in dermatomyositis, (d) fibrosis of the lung in generalized scleroderma; 2. hemosiderosis of the lung (anaphylactoid purpura of the interstitial lung tissue); 3. reticulosis of the lung? (proliferation of the reticuloendothelial system); 4. lymphogranulomatosis of the lung.

D. *Lipoidoses:* interstitial fibrosis in Gaucher's disease.

E. *Malformations of the interstitial tissue of the lung of neoplastic type:* 1. angioreticulosis; 2. reticulosarcoma; 3. leukemic infiltration.

Addendum: "azotemic edema," interstitial lung edema in acute glomerulonephritis.

Roentgenographically, the interstitial processes first produce a ground glass resemblance with a reticular pattern usually apparent within the hazy areas, the latter becoming more evident after prolonged illness. Dovetail like or star-shaped opacities appear at points of intersection in the reticulum. If exudate or transudate in the alveoli is present, focal opacities result which are almost indistinguishable from those seen in partial atelectasis. The lesions are more apparent near the hilus, similar to central bronchopneumonia, with large emphysematous areas present in most cases. Finally, right heart failure results in pulmonary congestion and enlargement of the heart, particularly the right atrium and pulmonary arch.

Azotemic edema, inflammation resulting in interstitial disease, hypersensitivity reactions and malformations of the interstitial tissue of the lung are discussed in greater detail with several case histories presented.

In concluding, the author states that the purpose of his presentation has been to emphasize the significance of interstitial lung diseases in childhood and to pose problems rather than solve them, and thus stimulate further investigation.—*Daniel L. Rousseau, M.D.*

Kaniak, E. G., and Kümmerle, F. Intrabronchiales Chondrom. (Intrabronchial chondroma.) *Thoraxchirurgie*, July, 1959, *7*, 27–34. (From: Chirurgische Universitätsklinik, Freiburg i. Br., Germany.)

Of 452 tumors of lungs and bronchi seen during eight years in the authors' clinic, 97.5 per cent were carcinomas. There were also 7 bronchial adenomas, 3 hamartomas and 1 intrabronchial chondroma.

The clinical, roentgenologic, bronchoscopic, and surgical findings in the case of intrabronchial chondroma are given in some detail. The anatomic-microscopic diagnosis is discussed.—*H. W. Hefke, M.D.*

Arnois, Dolores-Crystal, Silverman, Frederic N., and Turner, Malcolm E. The radiographic evaluation of pulmonary vasculature in children with congenital cardiovascular disease. *Radiology*, May, 1959, *72*, 689–698. (Address: F. N. Silverman, Children's, Hospital, Cincinnati 29, Ohio.)

The authors report an interesting study undertaken in an effort to evaluate the ability to appreciate increased or decreased pulmonary vascularity on conventional roentgenograms of the chest in children with congenital cardiovascular malformations of a known nature. Three readers, all radiologists with different types of experience—university hospital, private hospital, and private practice—read the films. A total of 128 films were involved. Sixty-four were normal, 32 had overvascularity and 32 had undervascularity. Each film was read three times at several weeks' intervals and the readers did not know they were rereading the same films. The mechanics of the study and the statistical analysis of the results are gone into in detail in the article.

The results indicated that there was a high degree of internal consistency. In other words, there was no more than chance variation between the different readers or between the different readings on the part of any one of the three readers in evaluating this series of films. A distinct difference was found, however, in the number of errors related to the recognition of pulmonary undervascularity in comparison with the recognition of pulmonary overvascularity. Out of the total of 290 errors for all three readings,

243, or 84 per cent, were due to the difficulty in distinguishing between normal and decreased vasculature. This contrasted to a total of only 38, or 13 per cent of all errors, due to failure to differentiate between normal and increased vascularity. In evaluating the errors by diagnosis it was found that in the group of patients with known pulmonary overvascularity there were 24 errors out of 288 readings, or 8 per cent, while in those with known undervascularity there were 136 errors out of 288 readings, or 47 per cent.

These findings show that it is apparently much easier to recognize pulmonary overvascularity than pulmonary undervascularity in children with congenital malformations of the heart.—*Donald N. Dysart, M.D.*

Hodgson, Corrin H., Burchell, Howard B., Good, C. Allen, and Clagett, O. Theron. Hereditary hemorrhagic telangiectasia and pulmonary arteriovenous fistula. *New England J. Med.*, Sept. 24, 1959, *261*, 625–636. (From: Section of Medicine, Section of Roentgenology and Section of Surgery, Mayo Clinic and Mayo Foundation, Rochester, Minn.)

This is an interesting and comprehensive report on 231 members of a large family in which it was found that 39.4 per cent had hereditary telangiectasia. Both sexes were affected in about equal numbers and both were equally capable of transmitting the disease to their offspring. A significant number of the family suffered from important complications of telangiectasia, such as bleeding and disturbance of the central nervous system. Fourteen of the 231 had pulmonary arteriovenous fistulas. Six of theses 14 cases had symptoms from the fistula.

Pulmonary arteriovenous fistula is a serious part of a generalized vascular dysplasia. It may cause distressing symptoms, may require surgical removal or may endanger the life of the patient. All families known to have hereditary telangiectasia should have periodic roentgen studies of the thorax in search for fistulas whether there are symptoms or not. The only satisfactory treatment for pulmonary arteriovenous fistula is surgical excision; no more lung tissue should be removed than is necessary because other fistulas may develop subsequently and require excision. All fistulas do not need to be excised, but surgical intervention may appear indicated in the presence of enlarging lesions, hemoptysis, hemothorax, polycythemia, bloodstream infections and abscesses.

It is concluded that 2 persons having hereditary telangiectasia should not marry each other and have children, for a lethal form of the disease is likely to be transmitted to the children.

The authors give a comprehensive study of the etiology, which is unknown, clinical aspects, clinical laboratory findings, roentgenologic aspects and treatment of this disease. There is a very complete bibliography.—*Peter C. Truog, M.D.*

Sammons, Billy P. Arteriovenous fistula of the lung. *Radiology*, May, 1959, *72*, 710–715. (Address: U. S. Naval Hospital, Pensacola, Fla.)

The existence of pulmonary arteriovenous fistula as an entity was first reported by Smith and Horton in 1939. Since that time 200 cases have been reported in the literature. The present article gives a résumé of the diagnosis and management of this condition. A brief review of the pertinent literature is included and 3 case histories are discussed.

In the past seven years, 8 cases of arteriovenous fistula of the lung have been diagnosed and operated upon at the St. Albans Naval Hospital, St. Albans, New York. Seven of these were males and all were of the Caucasian race. The reported cases, however, did not show any significant sex or race predilection. Fifteen per cent had a familial history of Rendu-Osler-Weber's disease and 40 per cent had telangiectatic lesions elsewhere in the body. Dyspnea was present in less than one third of the reported cases.

Clinically, the uncomplicated cases are asymptomatic. Physical findings consist of clubbing of the fingers and toes and a bruit over the site of the anomaly. Polycythemia is found in a high percentage of patients. The complications are commonly neurologic in nature, consisting of brain abscesses, acute meningo-encephalitis and cerebral thrombosis, the latter on the basis of the existing polycythemia.

In cases with the above complications, the clinical findings along with the roentgen findings of a solitary density in the chest may suggest pulmonary carcinoma with intracranial metastases. Because of this similarity and because of the differences in management, it is important that careful roentgenologic distinction be established. The most characteristic roentgen picture is that of a spheroid density anywhere in the lung with prominent vascular connections. Laminagrams will usually reveal afferent and efferent vessels in relationship with the anomaly. Calcification is rare. Fluoroscopically, pulsations and changes in size of the lesion may be detected with the Müller and Valsalva procedures. The former increases and the latter decreases the size, due to changes in intrathoracic pressure. If the possibility of fistula has not been excluded by these procedures, or if a fistula is definitely established, angiocardiography should be performed. By this means the exact vascular connections are outlined and the systemic feeders or chest wall involvement by the fistula can be detected. Hamartomas have presented the largest number of suspicious roentgenograms, necessitating angiocardiography to exclude a pulmonary vascular malformation.

The lesions are usually just beneath the visceral pleura. About 20 per cent are bilateral or involve two lobes on the same side. The arterial and venous con-

nections are usually from the pulmonary artery and vein of the involved lobe, but they may be from the vessels of an adjoining lobe, the aorta, or the intercostal vessels. Some have a completely anomalous vascular supply and drainage system.

Because of the serious complications which may occur, surgery is recommended even in asymptomatic individuals.—*Z. Petrany, M.D.*

Tori, Giulio, and Garusi, Gianfranco. Congenital absence of right pulmonary artery with patent ductus arteriosus and auricular septal defect. *Radiol. clin.*, July, 1959, *28*, 228–250. (From: Radiology Institute of Bologna University, Bologna, Italy.)

About 80 instances of congenital absence of a pulmonary artery have been reported. It may occur either as an isolated anomaly or associated with other defects of cardiac cavities or of the large vessels.

A brief summary of the embryology relevant to normal development of the cardiopulmonary system is presented. Suggestions of the mechanism of causation of the anomaly are also made.

The patient reported is a twenty-seven year old female with a history of mild dyspnea on exertion and occasional hemoptysis. Exhaustive clinical laboratory studies pertinent to the case are revealing. The case was examined by plain roentgenography of the chest, frontal and sagittal laminagraphy, fixed and moving roentgen kymography, angiocardiography, and bronchospirometry.

Diagnosis is established on the basis of a variety of tests and observations. (1)The plain roentgenograms usually show, on the affected side, a smaller hemithorax, smaller rib interspaces, an elevated diaphragm, and increased radiolucency of the lung. Discrepancy in vascular markings is the most valuable sign. Laminagraphy may demonstrate the true condition of the hilus. (2) The electrocardiogram usually is abnormal with evidence of right ventricular hypertrophy. (3) Cardiac catheterization studies may reveal abnormalities. (4) Angiocardiography has given an exact diagnosis in about 30 cases, the authors state, and has been the method used in most cases reported in recent reviews. (5) Hemoptysis is a frequent complication. (6) Collateral circulation usually is affected by the bronchial arteries; direct from the innominate artery or ascending aorta; anastomosis with the intercostal arteries. (7) Studies of respiratory function show that vital capacity of the lung on the affected side almost always is reduced.—*David C. Alftine, M.D.*

Vickers, Charles W., Kincaid, Owings W., Ellis, F. Henry, Jr., and Bruwer, Andre J. Left atrial calcification. *Radiology*, April, 1959, *72*, 569–575. (Address: C. W. Vickers, Mayo Clinic, Rochester, Minn.)

Five cases are presented in which calcification of the left atrium was noted roentgenologically. All 5 patients had severe rheumatic heart disease with involvement of the mitral valve. Pure mitral stenosis was present in 4 cases. In the fifth case there was severe mitral insufficiency. Mitral commissurotomy was performed in 4 cases.

All recorded cases, including those presented by the authors, have been associated with rheumatic heart disease of long standing. It may, therefore, be assumed that left atrial calcification is pathognomonic of that condition. The calcification may occur in the endocardium or in the subendochondral region or within a mural thrombus. The body of the left atrium and the left auricular appendage are involved in the process with approximately equal frequency.

Roentgenology affords the only means for diagnosing this condition clinically. On the roentgenogram, left atrial calcification appears as a curvilinear density up to 2 mm. in thickness in the region of the wall of the left atrium. This shell-like calcification may involve a large portion of the wall or it may be small and sickle shaped. Lamination or unusual thickness of the calcified layer is suggestive of calcification of a thrombus. The calcification may not be observed on the conventional chest roentgenogram. It is best demonstrated by roentgenoscopy, by roentgenograms in the right anterior oblique and lateral projections, or by overpenetrated Bucky films. Laminagrams may be necessary for clearer visualization.

Left atrial calcification must be differentiated from calcification of other intracardiac structures: (1) pericardium, (2) coronary artery, and (3) cardiac valve. Calcification of extracardiac structures, such as hilar lymph nodes, costal cartilages, and intrathoracic cysts and tumors, as well as intracardiac tumors and ventricular aneurysms must be excluded.

The presence of large amounts of calcium in the wall of the the left atrium presents technical problems for the surgeon in his operative approach to the mitral valve. Its recognition is of importance, therefore, in establishing the decision of operability.—*Arno W. Sommer, M.D.*

Stecken, A., and Weiss, U. Die Tomographie der Aortenisthmusstenose; röntgenanatomische Studie an 57 Schichtuntersuchungen. (Laminagraphy of aortic coarctation; roentgen anatomic study in 57 cases.) *Fortschr. a. d. Geb. d. Röntgenstrahlen u. d. Nuklearmedizin*, Aug., 1959, *91*, 152–171. (From: Röntgenabteilungen der I. Medizinischen Universitätsklinik und Poliklinik der Charité, Berlin, Germany.)

Angiocardiography is recognized as a very reliable diagnostic procedure for patients with suspected aortic coarctation. In view of its possible complica-

tions (especially cerebral) the authors examined a series of patients by laminagraphy.

Laminagrams are made in the anteroposterior as well as in the lateral and left anterior oblique projections with barium in the esophagus.

In patients with coarctation the following findings are present in the anteroposterior projection: (a) a definite notch at the left lateral border of the aorta just below the aortic arch (not present when marked elongation of the aorta has occurred); (b) poststenotic dilatation of the descending aorta (common); (c) some ectasia of the ascending aorta and the brachiocephalic arteries (not constant); and (d) deviation and indentation of the barium filled esophagus.

On lateral and oblique laminagrams, coarctation may cause the following manifestations: (a) a narrowing at the site of the coarctation; (b) poststenotic dilatation of the descending aorta displacing the esophagus anteriorly; (c) dilated brachiocephalic vessels (common); and (d) dilated, tortuous intercostal arteries (not constant).

The coarctation could be demonstrated by laminagraphy in all the cases presented in this study; the findings were verified either by surgery or subsequent aortography. However, the authors admit that laminagraphy can not match the contrast achieved with angiocardiography.—*Wolfgang H. Steinmetz, M.D.*

Chiche, P., Najean, Y., and Acar, J. Dilatation et visibilité radiologique de l'oreillette gauche au cours de cardiopathies non mitrales. (Dilatation and radiologic visibility of the left atrium in cases of nonmitral cardiopathy.) *Presse méd.*, May 27, 1959, *67*, 1072–1074. (From: Service de Cardiologie de l'Hôpital Lariboisière, Paris, France.)

The prevalent roentgen sign of mitral stenosis, in the posteroanterior view, is doubling of the right border of the heart superiorly and, less frequently, bulging of the left border immediately above the atrioventricular junction (G point). The oblique views are not as helpful as the frontal or posteroanterior view.

Of 125 cardiac patients investigated, the authors found 28 cases of left atrial dilatation with no mitral disease. Thirty-five patients had constrictive pericarditis; of these, 10 had definite enlargement of the left atrium and 11 had somewhat doubtful roentgen evidence of dilatation. Forty patients had left ventricular insufficiency on the basis of either postcoronary myosclerosis or arterial hypertension; of these, 10 showed gross dilatation of the left atrium and 4 had probable dilatation. Another 40 patients with aortic valvular disease affecting the left ventricle were divided into two groups: 20 had left ventricular insufficiency and, of these, 7 showed left atrial dilatation; the remaining 20, who did not have any demonstrable left ventricular insufficiency, showed no left atrial dilatation with the exception of one single case.

The authors conclude from these observations that left atrial dilatation in the absence of mitral disease is closely related to left ventricular pathology and function.—*Jirair N. Sarian, M.D.*

Uricchio, Joseph F., Lehman, J. Stauffer, Fitch, Edward A., Brest, Albert N., Boyer, Randal A., and Likoff, William. The diagnosis of traumatic mitral regurgitation by cardiac ventriculography. *Am. J. M. Sc.*, July, 1959, *238*, 73–78. (From: Department of Medicine, Department of Radiology, Department of Thoracic Surgery, Hahnemann Medical College and Hospital and the Bailey Thoracic Clinic, Philadelphia, Pa.)

The authors report 4 cases in which traumatic mitral regurgitation occurred following mitral commissurotomy for tight mitral stenosis. In all of these cases the clinical findings were confirmed by cardiac ventriculography. Concentrated radiopaque material was injected rapidly into the left ventricle through a needle inserted through the lower anterior chest wall directly into the ventricle. In each case there was immediate extensive regurgitation of the contrast medium into the left atrium. The roentgenograms were taken in a lateral projection.

All cases were operated on again and each showed a tear in the septal leaflet and marked mitral regurgitation. Each one was successfully repaired. Cardiac ventriculography was performed on one of these postoperatively and no significant regurgitation was present.

Cardiac ventriculography permits differentiation between significant and insignificant mitral insufficiency.—*Frank M. Windrow, M.D.*

MISCELLANEOUS

Scott, Wendell G. The clinical radiologist and the problems of radiation hazards. *J.A.M.A.*, May 23, 1959, *170*, 421–428. (Address: 100 N. Euclid Ave., St. Louis 8, Mo.)

The advent of the atomic industrial revolution has produced in the public an awareness of ionizing radiations and, as a result, many people are confusing thermonuclear radiation and whole body radiation with other facets of radiation, such as diagnostic roentgenology. Diagnostic roentgenology has had a marked growth because of the contributions it has made to the health and well-being of mankind. Approximately 38 million roentgenographic examinations are made each year, most of them on the sick who are over thirty years of age.

The deleterious effects of ionizing radiation should be considered to enable those using radiation to help prevent these effects. The deleterious effects can be separated into the somatic and genetic effects. Total

body irradiation by either a large single dose or cumulative doses causes an increased risk in developing leukemia. Sufficiently large doses of radiation can shorten the life span by accelerating the aging processes. Unnecessary exposure to radiation should be avoided. Mutations have been produced experimentally by irradiating fruit flies and mice. This information has been extrapolated to humans. The mutations produced by irradiation are the same as those produced by other agents. They are usually recessive. The Committee on Genetic Effects of Atomic Radiation of the National Academy of Sciences recommends that, during the first thirty years of life, the average gonadal dose for large populations not exceed 10 r of man made radiation plus 4.3 r from natural background sources. The total body radiation from diagnostic roentgenology is rather negligible as to the somatic effect; the important factor is the gonadal dose in those under thirty years of age.

The gonadal radiation dosage from medical use of roentgen rays can be reduced from 75 to 85 per cent without impairing the efficiency of the diagnostic examination. The examination should be performed by physicians trained in radiology and by experienced x-ray technicians. The examination should be carefully done. A radiation physicist should check the layout. The technicians should be taught the importance of lowering the gonadal exposure and of using gonadal shielding devices. The quantity of the beam can be reduced and the quality improved by means of filtration. A 2 mm. Al filter should be used on the roentgenographic tube and a 3 mm. Al filter on the fluoroscopic tube. Collimated beams, fast films and screens and special developing agents can reduce the amount of radiation needed. Fluoroscopic image intensifiers also reduce the amount of radiation. Delaying pelvic measurements and examinations on pregnant women until the last trimester reduces the chance of affecting the developing fetus.

Every physician using diagnostic radiation should keep the radiation dosage to the gonads to the lowest level possible. The key to the safe use and control of medical radiation lies in the education of the physician in the fundamentals of genetics, radiobiology and radiology.—*Charles W. Cooley, M.D.*

Miller, Jarrell E., and Swindell, Gerald E. Common sense in the diagnostic use of x-ray. *J.A.M.A.*, June 13, 1959, *170*, 761–765. (Address: J. E. Miller, 3500 Gaston Ave., Dallas, Texas.)

This article is a timely warning against hysterical or irresponsible statements concerning the use of ionizing radiation in medicine. Ionizing radiation is a double-edged sword; it has power for good and can cause harm. But modern life has many dangers, most of which are double-edged swords. Without fire, our civilization would not exist, but it has power for harm. The motor car has had a profound effect upon our entire civilization, and yet at considerable cost in human life. It seems not to have been generally understood that the human race has been subject to background radiation from natural sources throughout its existence.

The authors point out that diagnostic exposures are, in general, partial body exposures. It would be the rare person who might receive enough radiation to cause even the slightest demonstrable body harm. Examinations where this might occur are calculated risks, just as are operative procedures, which patients agree to take. If the use of radiation is to occupy its proper place in the practice of medicine, its hazards should be stressed to any physician who presumes to use it and its benefits should be stressed to the public. It is the physician's responsibility, and indeed his prerogative, to use judgment in the application of any hazardous medical procedure to a human being. No one else should have this exclusive privilege. Any practitioner who uses radiation with conservative judgment and skill should not be made to feel uneasy about its use. Data given to us by geneticists, radiation biologists, and physicists are important contributions to basic science and should be viewed in that perspective. Viewed in the larger perspective, roentgen rays used in medical diagnosis are not harmful; they are beneficial.—*Douglas S. Kellogg, M.D.*

Cooper, George, Jr., and Williams, Kenneth. Radiation dosage to female gonads during diagnostic roentgenographic procedures. *J.A.M.A.*, June 13, 1959, *170*, 766–768. (From: The Department of Radiology, University of Virginia Hospital and School of Medicine, Charlottesville, Va.)

It is noted that during recent years a great deal has been written about the hazards involved in using roentgen rays to examine human beings for purposes of medical diagnosis. While many data have been accumulated, there is still considerable disagreement as to the interpretation of the data and it is not possible to define with any exactness the risk accepted when any individual patient is advised to have a particular roentgen-ray examination. Until the danger levels can be determined accurately, a conservative course should be followed. In medical diagnosis, radiation should be used purposefully and the value of the information sought should outweigh the estimated hazard.

Because of the relative unimportance of the somatic hazard and the ease of avoiding testicular exposure, in the well-run department of radiology concern about the genetic hazards of roentgen diagnosis can be focused on a limited number of procedures in which the beam of radiation must be passed through or near the ovaries of female patients still within the child bearing age. The genetic significance of this

radiation is uncertain, but experience indicates that, assuming only essential examinations are performed during pregnancy, the greatest opportunities for reducing ovarian dosage lie in strict evaluation of the need for roentgenographic investigation of the gastrointestinal tract, the gallbladder, and the lumbar spine in young women, and for repeated roentgenograms in the handling of hip disease in young girls.

Roentgen-ray examinations which involve irradiation of the pregnant uterus usually involve direct irradiation of the fetal gonads. It has been estimated that the gonads of a male fetus in a vertex presentation may receive from 2 to 4 rad during roentgenography of the pregnant uterus. A number of factors combine to indicate particular caution in subjecting the pregnant uterus to roentgenographic examination. The thickness and volume of the part necessitate heavy exposure for adequate penetration. The maternal gonads must be exposed, the fetal gonads must usually be exposed, and often the entire fetus must be irradiated. It is clear that during pregnancy only essential roentgenographic procedures should be performed.

The authors include tables of ovary dose per exposure, and of age distribution of roentgenographic procedures involving significant ovarian dosage, as developed at the University of Virginia Hospital in 1957.—*Douglas S. Kellogg, M.D.*

Hodges, Paul C. The radiologist looks at radiation hazards. *Radiology*, April, 1959, *72*, 481–488. (Address: 950 East 59th St., Chicago 37, Ill.)

Geneticists, biophysicists and radiologists are essentially in agreement about genetic and other health hazards of ionizing radiations and the methods needed to reduce these hazards to a minimum.

It has not been shown that the extremely small tissue doses delivered in properly conducted roentgen examinations increase the mutation rate or the incidence of leukemia, or shorten the life span, but there is every reason to believe that with larger doses these effects can be produced. Our policy, therefore, should be to avoid unnecessary examinations, to take every practical precaution to keep doses to a minimum, to allay public hysteria, and to emphasize the fact that when the work is done by a competent radiologist the health risk to the patient and his progeny can be kept very small relative to the benefit of the examination.

Unnecessary examinations should be avoided and all possible safeguards must be built into roentgen-ray apparatus and incorporated into roentgenologic techniques. It is particularly important to shield the gonads from the direct roentgen-ray beam whenever possible. In making roentgenograms of the pelvis or the urinary tract, adequate shielding can reduce the testicular dose to approximately 5 per cent of what it would be without the shield. Higher voltages and heavier filtration can effect a reduction of tissue dose of about 50 per cent without loss of film quality. Fast screens and fast films, properly exposed and fully developed, may result in slight loss of technical excellence but can bring about a substantial reduction in tissue dose. Rectangular ports, to restrict the incident beam to the absolute minimum needed to include the film being used, should replace the customary round ports. This will result in improvement in the quality of roentgenograms and substantial reduction in the amount of tissue irradiated. The employment of small rectangular ports is of particular importance in fluoroscopy and spot filming.—*Arno W. Sommer, M.D.*

Powell, Clinton C. The government looks at radiation hazards. *Radiology*, April, 1959, *72*, 489–492. (Address: National Institutes of Health, Bethesda, Md.)

The author discusses the problems of radiation hazards as seen in the Department of Health, Education and Welfare. These problems have been brought to the fore because of increasing public interest and concern due to newer scientific information concerning possible deleterious effects of low-level radiation exposure and the rapid expansion of radiation sources.

It is felt that any Government programs will be most meaningful and helpful if they are based on a spirit of mutual assistance and cooperation with appropriate professions. Any ill-advised and ill-considered action could be avoided by securing the advice, guidance and mature judgment of practitioners, their organizations, and other competent professional individuals. The Government should not attempt to regulate the practice of radiology or to control any clinical procedures by legislation or inspection as the medical profession would not tolerate it. On the other hand, some official control over the installation of potential radiation hazards and the disposal of obsolescent equipment would probably be welcomed. Radiologists in particular can do much to help provide accurate information to the general public as part of a public education program. This would do much to counteract some of the inflammatory, scientifically misleading, or inaccurate articles that have appeared in some nonscientific publications.

The Government in return can be of help in the support of research programs, in public education, in the maintenance of equipment in the safest operating condition, and in providing a legal basis for exclusion of the untrained and incompetent individual from using a potentially hazardous piece of equipment.—*Donald N. Dysart, M.D.*

Webster, Edward W. Hazards of diagnostic radiology: a physicist's point of view. *Radiology*, April, 1959, *72*, 493–507. (Address:

Department of Radiology, Massachusetts General Hospital, Boston 14, Mass.)

A constructive evaluation of diagnostic hazards should consider the following points: the relationship of dose to hazard for the individual, the dose and the hazard involved in a given examination, the likely benefit to the individual of a given examination, and the means of reducing the dose and, therefore, the hazard.

Regarding the relationship of dose to hazard, there are two possible views. The optimistic view holds that at the level of 1 r there is no hazard to an exposed individual *per se*. The pessimistic view is that at the level of 1 r there is a definite probability of permanent damage in terms of delayed effects on the individual, particularly as regards genetic damage. By applying certain statistical and experimental data, an attempt is made to quantitate carcinogenic and genetic effects of various diagnostic roentgenographic procedures within the limits of the pessimistic assumptions. It is concluded that there is an extremely low level of personal risk that attends all roentgenographic examinations, and although the risk of genetic damage is also small it is considerably larger in many examinations than the personal risk but becomes much less when there is protection to the gonads. However, the somewhat larger genetic hazards of most examinations are surpassed by those accruing from wearing a radium dial wrist watch and, apparently, from wearing trousers, according to the data presented.

Since the hazards, even at worst, are very small and are mainly to posterity, the benefits anticipated from a diagnostic examination do not have to be very large. In the case of mass chest surveys, a quantitative comparison of benefit and damage is theoretically possible; a preliminary consideration indicates a large balance of benefit if well-coned roentgen-ray apparatus is used.—*Walter H. Jarvis, Jr., M.D.*

Schull, William J. A geneticist looks at the radiation hazard. *Radiology*, April, 1959, *72*, 522–534. (Address: Department of Human Genetics, University of Michigan Medical School, Ann Arbor, Mich.)

The radiologist has been keenly aware for some time of the potential somatic damage to his patients and to himself stemming from roentgen irradiation, and more recently there has been an increased awareness of the potential genetic damage. However, in general this has been directed toward individuals rather than populations. The geneticist, on the other hand, tends to think in terms of populations, or pools of genes. Therefore, he may view as suspect a procedure which, while altering the individual risk by only an infinitesimal amount, may effect substantial damage at the population level solely because of the large number of individuals at risk.

Through the experimental work of numerous investigators on a wide variety of infrahuman forms ranging from bacteria to the mouse, it has been demonstrated that, following exposure to ionizing radiation, the yield in gene mutation is linearly related to dose, and it is independent of the intensity of the exposure; *i.e.*, the effects of repeated exposure are cumulative. The experimental evidence for linearity rests largely on moderate to high doses (25 r and up) but is sufficiently extensive within this range for geneticists to accept, in general, the point of view that "there is no known threshold of radiation exposure below which genetic damage does not occur." There is, however, some controversy at present regarding the independence of the intensity of exposure.

Regardless of whether intensity of exposure is or is not a factor to be reckoned with, an appraisal of the potential damage done a human population by exposure to a given dose of radiation involves many unknowns. The ionizing radiation to which we are or may be subject stems from four sources; namely, (a) background, (b) the fall-out from weapons-testing, (c) the use in medicine of roentgen radiation and radioactive isotopes, and, for a small segment of the population, (d) occupational hazards. Disregarding occupational hazards, the "average" dose of radiation experienced in thirty years, which would be the exposure accumulated to approximately the midpoint of the reproductive span, would be in the neighborhood of 7 to 8 rad with medical uses accounting for over half of this amount.

Data available on human populations for appraising the genetic hazards are scanty, being limited to six studies thus far. None of the studies has reported significant differences between exposed and nonexposed populations with respect to mortality, birth weight, and anthropometry. Although the incidence of congenital malformations following parental exposure is controversial, it is doubtful that any increase in congenital malformations following parental exposure has yet been demonstrated. Sex ratio studies show an effect consistent with genetic notions but it is not proved that the results *must* be due to the operation of sex-linked lethal mutants.

"Permissible doses" represent an effort to equate the potential benefits from the uses of ionizing radiation with the possible damage it may produce; however, recommendations in the light of our present knowledge cannot be especially precise. Certainly until such time as more information is available, we should limit our exposure as much as is consistent with the practice of good medicine.—*Walter H. Jarvis, Jr., M.D.*

Kaplan, Ira I. Genetic effects in children and grandchildren of women treated for infertility and sterility by roentgen therapy; report of a study of thirty-three years. *Radi-*

ology, April, 1959, *72*, 518–521. (Address: 755 Park Avenue, New York 21, N. Y.)

The present study is an analysis of the genetic changes observed in two successive generations of the offspring of 644 women who had received roentgen therapy. The tissue dose was approximately 65 r to the ovaries and 90 r to the pituitary; the follow-up was from one to thirty-three years and, in over 50 per cent of the cases, from five to thirty-two years.

Of the 351 irradiated women who conceived, 318 bore 566 children. There are 543 normal healthy living children. Twenty children died at or after birth, including 8 stillbirths and 12 deaths of living children, and 3 children are alive with abnormalities. In this series the fetal death rate is 20.6 per cent compared with the 16.6 per cent of the Office of Vital Statistics; however, it should not be overlooked that these women were not deemed normal before therapy. There were 91 women who miscarried 123 times, but 68 of these again normally conceived and bore children. At present 35 children of these irradiated women are married and 31 of these already have had a total of 46 normal children, that is, grandchildren of the originally irradiated women; one died shortly after birth as a result of maternal eclamptic toxemia.

In only 1 case has malignant disease followed irradiation for sterility, that being a twenty-six year old woman who was treated in 1948, failed to conceive, and died February 6, 1949, from leukemia. There has been no cancer or leukemia of any type noted in any of the children or grandchildren of the irradiated women over the course of the past thirty-three years. The incidence of genetic damage to the children and grandchildren of this group is less than that in the normal population. Some have stated that the series studied is too small to yield significant data. This may be true, but to the author the results are more impressive than the geneticists' calculations based on theory.—*Walter H. Jarvis, Jr., M.D.*

Court Brown, W. M., and Doll, R. Adult leukaemia; trends in mortality in relation to aetiology. *Brit. M. J.*, April 25, 1959, *1*, 1063–1069. (Address: W. M. Court Brown, Director of the Medical Research Council's Group for Research on the General Effects of Radiation, Western General Hospital, Edinburgh, Scotland.)

The authors reviewed the 1958 data on mortality due to leukemia presented by the Registrar-General of England and Wales. Believing that there is reason to suppose a different causation of acute versus chronic leukemia types, the authors re-analyzed the previous data to find if there are any trends in mortality for (a) chronic lymphatic, (b) chronic myeloid, and (c) all acute leukemias. The mortality for each of the three types was considered in each of three age groups, noting the trend both in regard to sex and change in time. Plasma-cell leukemia was excluded. The authors discuss the possible error due to reports of "unclassified" leukemia.

Numerous tables and graphs illustrate the data. In the periods 1945–1949 and 1955–1957, the male mortality from leukemia has increased at all ages. Below the age of sixty, the increase was about 25 per cent; at the age of seventy and above, the rate had more than doubled.

All three types of leukemia were represented in the increase for the older age groups. At ages under sixty years, the increase has largely been due to acute leukemia with a slight increase in chronic myeloid leukemia. Estimated mortality from chronic lymphatic leukemia at these ages remained practically constant.

Trends in mortality and the relationships between mortality and age were similar in both sexes, with an exception in chronic myeloid leukemia. At most ages, the sex ratio has had distinctive value for each of the three types of leukemia studied. All the ratios have increased since 1945–1949, but have maintained the same relative position.

The increased incidence of leukemia of all types in the older age groups was attributed partly to improved diagnosis and more accurate death certification. The possibility of a cohort factor complicating the data was emphasized.

The authors conclude that there is no real evidence of changing incidence of chronic lymphatic leukemia over the past thirteen years. The data were considered to be inconclusive with respect to chronic myeloid leukemia. There was, however, a real increase of acute leukemia mortality by one-third, at all ages under sixty-five in both sexes.

The authors also discuss briefly the etiologic relationships and suggest that the observed increase in age-specific death rates for acute leukemia at ages under sixty is largely real and due to increased exposure of the population to leukemogenic factors in the environment. That this is specifically due to radiation exposure, has already been suggested by studies of atomic bomb victims and radiation treated spondylitis. Unable to definitely incriminate increasing background radiation, the authors suggest the importance of the high rate of exposure to roentgen rays, *e.g.*, 40–100 r/min. (background radiation 2×10^{-6} r/min.).—*Roger A. Sterling, M.D.*

Ford, Dorothy D., Paterson, J. C. S., and Treuting, W. L. Fetal exposure to diagnostic x rays, and leukemia and other malignant diseases in childhood. *J. Nat. Cancer Inst.*, June, 1959, *22*, 1093–1104. (From: Department of Tropical Medicine and Public Health, Tulane University, New Orleans, La.)

The authors made a survey of the comparative incidence of exposure to antenatal radiation *in utero*

and of the occurrence of leukemia and other malignant diseases in later childhood. The case material consisted of deaths (which occurred before the age of ten years) from leukemia and other malignant diseases in Louisiana during the five year period 1951 through 1955. The control cases were deaths from other causes matched for age, sex, race and place of death. Information concerning the incidence of irradiation (diagnostic roentgenograms during the last trimester of pregnancy) was obtained from either the doctor who delivered the mother or from the institution in which the child was born. The incidence of roentgen-ray exposure was found to be as follows: leukemia, 26.0 per cent; malignant disease cases, 28.4 per cent; and control cases 18.3 per cent.

These findings are in substantial agreement with those of Stewart *et al.* in England. The findings lend emphasis to the need for minimizing exposure of the fetus to roentgen rays, by careful determination of the indications for antenatal roentgenography and by attention to the technical procedure.—*Frank J. Rigos, M.D.*

Snegireff, Leonid S. The elusiveness of neoplasia following roentgen therapy for thymic enlargement in childhood. *Radiology*, April, 1959, *72*, 508–517. (Address: 1 Shattuck St., Boston 15, Mass.)

The author gives a preliminary report of a study of 148 persons who received roentgen irradiation in childhood and infancy because of an enlarged thymus gland. Included in the study are a group of 23 untreated patients with thymic enlargement and a comparison group of 162 patients without detectable enlargement of the thymus.

Although 75 of the 148 treated patients have been followed for over a period of twenty years, no malignant neoplasms have been found. Two patients were found to have developed a benign thyroid condition; one had an adenoma and the other cystic disease. Three of the group died of a nonmalignant disease. In the control group of 162 patients, there were also no cancers found; 6 deaths in this group were all from a nonmalignant disease.

Since the previously reported high incidences of primary cancer of the thyroid and of leukemia following irradiation for thymic enlargement is not borne out so far by this study, the author mentions several factors which should be kept in mind in evaluating any reports. Variables such as age at the time of roentgen therapy, total roentgen dose, interval between multiple doses, duration and completeness of observations, sex of patient, the total time of follow-up, selection of comparison or control groups from particular geographic areas, general liability to risk of cancer in a particular primary site, and possible differences in economic status may each affect the results of any given study. Selection of patients, the composition of groups, the age at the time of treatment, and the dose given in different studies are thought to be the most important factors in causing the varied reported incidences.—*Donald N. Dysart, M.D.*

Stoloff, Irwin L., Haurani, Farid I., Repplinger, Evalyn F., and Havens, W. Paul, Jr. Effects of total-body irradiation on the production of antibody in man. *New England J. Med.*, June 18, 1959, *260*, 1258–1261. (From: The Departments of Medicine and Microbiology, Jefferson Medical College of Philadelphia, Philadelphia, Pa.)

There have been numerous studies in the past regarding the effects of whole body irradiation on the immunologic response of animals. Sublethal doses of radiation were found to inhibit antibody production and the maximum suppression of immunologic response was usually observed when the antigen was given twenty-four to forty-eight hours after irradiation. The anamnestic response was more radioresistant than the response to primary immunization.

There have been very few data on the effect of roentgen rays on the immunologic reponse in man. Collins and Brent showed that patients treated with 150 r total body radiation were able to produce tetanus antitoxin in normal amounts.

The authors undertook to study the immunologic response in 6 patients with acute leukemia and 1 patient with disseminated neuroblastoma. The patients were treated with whole body irradiation followed by infusion of homologous bone marrow. The object of the study was to determine whether the patients receiving varying dosages of radiation could produce antibodies to diphtheria toxoid and whether the infused homologous marrow cells could produce antibodies to tetanus toxoid in their new environment.

The qualitative or quantitative immunologic responses in 5 patients who were given 170 r to 490 r total body radiation were not significantly altered by the radiation. Two patients who were given 800 r total body radiation failed to produce antibodies. It could not be stated for a certainty that the radiation suppressed or delayed the antibody production, due to the small series.

The transfer of antibody-producing cells from donors to recipients as manifested by a measurable increase in circulating tetanus antitoxins was unsuccessful.—*Charles W. Cooley, M.D.*